Lucas, Z.
09/966746

(1)

STIC STN Search Report

09/966746

FILE 'HCAPLUS' ENTERED AT 10:31:10 ON 17 JUN 2002)

L1 3972 SEA FILE=HCAPLUS ABB=ON PLU=ON (INFECTIOUS OR INFECTION OR HIV OR HTLV OR AIDS OR HUMAN(3W)VIRUS OR ACQUIRED(2W) SYNDROM?) AND (CTL OR (CYTOTOX? OR CYTO TOX?)(W)T(W)(CELL OR LYMPHOCYT?))

L2 22 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 AND (HYBRIDIZ? OR HYBRIDIS?)

L2 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:123514 HCAPLUS
DOCUMENT NUMBER: 136:182454
TITLE: Methods for identifying and producing antigens for treating cancer and **infection**
INVENTOR(S): Zauderer, Maurice
PATENT ASSIGNEE(S): University of Rochester, USA
SOURCE: U.S. Pat. Appl. Publ., 54 pp., Division of U.S. Ser. No. 935,377.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002018785	A1	20020214	US 2001-822250	20010402

PRIORITY APPLN. INFO.: US 1997-935377 A3 19970922

AB The present invention relates to novel methods for the identification of antigens recognized by **cytotoxic T cells** (**CTLs**) and specific for human tumors, cancers, and infected cells, and the use of such antigens in immunogenic compns. or vaccines to induce regression of tumors, cancers, or **infections** in mammals, including humans. The invention encompasses methods for induction and isolation of **cytotoxic T cells** specific for human tumors, cancers and infected cells, and for improved selection of genes that encode the target antigens recognized by these specific T cells. The invention also relates to differential display methods that improve resoln. of, and that reduce the frequency of false positives of DNA fragments that are differentially expressed in tumorous, cancerous, or infected tissues vs. normal tissues. The invention further relates to the engineering of recombinant viruses as expression vectors for tumor, cancer, or infected cell-specific antigens.

L2 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:107056 HCAPLUS
DOCUMENT NUMBER: 136:166049
TITLE: Molecular vaccine linking intercellular spreading protein to an antigen
INVENTOR(S): Wu, Tzyy-Choou; Hung, Chien-Fu
PATENT ASSIGNEE(S): The John Hopkins University, USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009645	A2	20020207	WO 2001-US23966	20010801

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-222185P P 20000801
US 2001-268575P P 20010215
US 2001-281004P P 20010404

AB Superior mol. vaccines comprise nucleic acids, including naked DNA and replicon RNA, that encode a fusion polypeptide that includes an antigenic peptide or polypeptide against which an immune response is desired. Fused to the antigenic peptide is an intercellular spreading protein, in particular a herpes virus protein VP22 or a homolog or functional deriv. thereof. Preferred spreading proteins are VP22 from HSV-1 and Marek's disease virus. The nucleic acid can encode any antigenic epitope of interest, preferably an epitope that is processed and presented by MHC class I proteins. Antigens of pathogenic organisms and cells such as tumor cells are preferred. Vaccines comprising HPV-16 E7 oncoprotein are exemplified. Also disclosed are methods of using the vaccines to induce heightened T cell mediated immunity, in particular by **cytotoxic T lymphocytes**, leading to protection from or treatment of a tumor.

L2 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:364686 HCAPLUS
DOCUMENT NUMBER: 135:2592
TITLE: Transcriptional regulation of the urease operon in Helicobacter pylori in response to pH and mechanisms of stable colonization in the stomach
AUTHOR(S): Shirai, Mutsunori
CORPORATE SOURCE: Dep. Microbiol. Reprod., Pediatr. Infect. Sci., Yamaguchi Univ. Sch. Med., Ube, Yamaguchi, 755-8505, Japan
SOURCE: Yamaguchi Igaku (2001), 50(2), 593-601
CODEN: YIKUAO; ISSN: 0513-1731
PUBLISHER: Yamaguchi Daigaku Igakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review with 26 refs. Helicobacter pylori is known to colonize in the human stomach by neutralizing acidic condition with urease activity. The effect of acid on the transcription of the urease operon was investigated to det. whether H. pylori is has a novel mechanism under such conditions. We investigated the transcription of the urease gene cluster ureABIEFGH in Helicobacter pylori to det. the regulation of gene expression of the highly produced enzyme urease. Northern blot **hybridization** anal. demonstrated that cells of the wild-type strain grown in an ordinary broth had

transcripts of ureAB, ureABI, ureI, ureIE' and ure'FGH, but cells of a ureI-disrupted mutant had only the ureAB transcript. When the wild-type cells were exposed to pH 8 for 30 min, very little mRNA was detected. However, when exposed to pH 6, a large amt. of the ureIE" transcript, which was longer than the ureIE' transcript, together with the addnl. transcripts ureABIEFGH and ure'EFGH were detected. Rifampicin addn. expts. demonstrated that urease mRNAs, and the ureIE' transcripts in particular, are more stable at pH 5.5 than at pH 7. In accord with these results, urease activity in the crude cell ext. of the pH 5.5 culture was twice as much as that of the pH 7 culture, although the amts. of UreA and UreB detected by immunoblot anal. were similar. The transcription start point of ureI was identified by primer extension using a ureA promoter-deleted mutant, and a consensus sequence of RpoD-RNA polymerase was found in the ureI promoter. The 3' end of the ureIE" mRNA, detd. using S1 nuclease mapping, revealed that the transcript is able to cover the majority of the ureE open reading frame (ORF) that might be sufficient for UreE activity. Based on the above results, we conclude that the urease gene cluster of H. pylori consists of two operons, ureAB and ureIEFGH, and that primary transcripts of the latter as well as the read-through transcript, ureABIEFGH, are cleaved to produce several species of mRNA. It has been suggested that the ureIEFGH operon is regulated post-transcriptionally by mRNA decay in response to environmental pH. We are tempted to speculate that the ureE" transcript present in acidic pH may contribute to produce an active product that can proceed the nickel incorporation to the active center, the final step of urease biosynthesis. On the other hand, Th1 and Th2 cells play a central role in immunoregulation during **infection**. We show that H. pylori induces Th1 cytokine responses early (2 wk) but predominantly Th2 responses later (6 wk) in **infection**. The switch is principally mediated by urease-specific CD4(+) T cells, and correlates with a loss of urease-specific high-avidity JNK(+) Th1 and gain of low-avidity JNK(-) (possibly Th2) cells at the later stage of **infection**, concomitant wit ha 100-fold higher colonization level of H. pylori at 6 wk than at 2 wk that might tolerize high-avidity Th1 cells. Furthermore, differentiation of **HIV** gp160-specific CD4(+) Th and CD8(+) **cytotoxic T lymphocytes** (**CTL**) into effector cells is impaired in 6-wk H. pylori-infected mice immunized with vaccinia expressing gp160, and serum IL-12 stimulated by vaccinia **infection** is barely detectable. Adoptive transfer of urease-specific Th2 cells to mice infected only with gp160-expressing vaccinia abrogates Th1 polarization of the gp120 response, down-modulates virus-specific **CTL** responses, and delays virus clearance. Therefore, the H. pylori urease-mediated immunoregulation in the switch from JNK(+) Th1 to JNK(-) Th2 phenotype, and the preceding low IL-12 response, are likely crit. steps in the impairment of antiviral immunity. Other some novel mechanisms of H. pylori colonization and the strain diversity which we obtained were described and discussed in the text.

L2 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:785188 HCAPLUS
DOCUMENT NUMBER: 132:133037
TITLE: Molecular characterization of the guinea pig cytomegalovirus UL83 (pp65) protein homolog
AUTHOR(S): Schleiss, Mark R.; Mcgregor, Alistair; Jensen,

Nancy J.; Erdem, Guliz; Aktan, Laurie
CORPORATE SOURCE: Division of Infectious Diseases, Children's Hospital Research Foundation, Cincinnati, OH, 45229, USA
SOURCE: Virus Genes (1999), 19(3), 205-221
CODEN: VIGEET; ISSN: 0920-8569
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The tegument phosphoproteins of human cytomegalovirus (HCMV) elicit **cytotoxic T-lymphocyte** (CTL) responses and are hence candidates for subunit vaccine development. Little is known, however, about the tegument proteins of nonhuman cytomegaloviruses, such as guinea pig CMV (GPCMV). DNA sequence anal. of the Eco R I "C" fragment of the GPCMV genome identified an open reading frame (ORF) which is colinear with that of the HCMV tegument phosphoprotein, UL83 (pp65). This ORF was found to have identity to HCMV UL83 and was predicted to encode a 565-amino-acid (aa) protein with a mol. mass of 62.3 kDa. Transcriptional analyses revealed that a GPCMV UL83 probe **hybridized** with both 2.2kb and 4.2kb mRNA species at 48 h post-**infection** (p.i.); synthesis of these messages was blocked by phosphonoacetic acid (PAA), defining these as "late" gene transcripts. In vitro translation of the UL83 ORF in reticulocyte lysate resulted in synthesis of a 65 kDa protein. Immunofluorescence expts. revealed that the putative GPCMV UL83 homolog exhibited a predominantly nuclear localization pattern. Polyclonal antisera were raised against a UL83/glutathione-S-transferase (GST) fusion protein. This antibody identified a 70-kDa virion-assocd. protein, the putative GPCMV UL83 homolog, in immunoblot and radioimmunopptn. expts. Labeling expts. with 32P-orthophosphate indicated that the GPCMV UL83 protein is phosphorylated. Western blot anal. of glycerol tartrate gradient-purified virions and dense bodies confirmed that the putative GPCMV UL83 homolog was a constituent of both fractions.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:745332 HCAPLUS
DOCUMENT NUMBER: 130:94379
TITLE: Inactivating mutations in an SH2 domain-encoding gene in X-linked lymphoproliferative syndrome
AUTHOR(S): Nichols, Kim E.; Harkin, D. Paul; Levitz, Seth; Krainer, Michael; Kolquist, Kathryn Ann; Genovese, Cameo; Bernard, Amy; Ferguson, Martin; Zuo, Lin; Snyder, Eric; Buckler, Alan J.; Wise, Carol; Ashley, Jennifer; Lovett, Michael; Valentine, Marcus B.; Look, A. Thomas; Gerald, William; Housman, David E.; Haber, Daniel A.
CORPORATE SOURCE: Massachusets General Hospital Cancer Center, Harvard Medical School, Charlestown, MA, 02129, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(23), 13765-13770
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal
LANGUAGE: English
AB X-linked lymphoproliferative syndrome (XLP) is an inherited immunodeficiency characterized by increased susceptibility to Epstein-Barr virus (EBV). In affected males, primary EBV **infection** leads to the uncontrolled proliferation of virus-contg. B cells and reactive **cytotoxic T cells**, often culminating in the development of high-grade lymphoma. The XLP gene has been mapped to chromosome band Xq25 through linkage anal. and the discovery of patients harboring large constitutional genomic deletions. The authors describe here the presence of small deletions and intragenic mutations that specifically disrupt a gene named DSHP in 6 of 10 unrelated patients with XLP. Ths gene encodes a predicted protein of 128 amino acids composing a single SH2 domain with extensive homol. to the SH2 domain of SHIP, an inositol polyphosphate 5-phosphatase that functions as a neg. regulator of lymphocyte activation. DSHP is expressed in transformed T cell lines and is induced following in vitro activation of peripheral blood T lymphocytes. Expression of DSHP is restricted in vivo to lymphoid tissues, and RNA in situ **hybridization** demonstrates DSHP expression in activated T and B cell regions of reactive lymph nodes and in both T and B cell neoplasms. These observations confirm the identity of DSHP as the gene responsible for XLP, and suggest a role in the regulation of lymphocyte activation and proliferation. Induction of DSHP may sustain the immune response by interfering with SHIP-mediated inhibition of lymphocyte activation, while its inactivation in XLP patients results in a selective immunodeficiency to EBV.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:463998 HCAPLUS
DOCUMENT NUMBER: 129:188277
TITLE: Intestinal intraepithelial lymphocytes are primed for gamma interferon and MIP-1.beta. expression and display antiviral cytotoxic activity despite severe CD4+ T-cell depletion in primary simian immunodeficiency virus **infection**
AUTHOR(S): Mattapallil, Joseph J.; Smit-Mcbride, Zeljka; Mcchesney, Michael; Dandekar, Satya
CORPORATE SOURCE: Department of Internal Medicine, Division of Infectious Diseases, School of Medicine, University of California, Davis, CA, 95616, USA
SOURCE: Journal of Virology (1998), 72(8), 6421-6429
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Intraepithelial lymphocytes (IEL) are a crit. effector component of the gut-assocd. lymphoid tissue (GALT) and play an important role in mucosal immunity as well as in the maintenance of the epithelial cell integrity and barrier function. The objective of this study was to det. whether simian immunodeficiency virus (SIV) **infection** of rhesus macaques would cause alterations in the immunophenotypic profiles of IEL and their mitogen-specific cytokine

(gamma interferon [IFN-.gamma.] and MIP-1.beta.) responses (by flow cytometry) and virus-specific **cytotoxic T-cell (CTL)** activity (by the chromium release assay). Virally infected IEL were detected through the entire course of SIV **infection** by in situ **hybridization**. Severe depletion of CD4+ single-pos. and CD4+CD8+ double-pos. T cells occurred early in primary SIV **infection**, which was coincident with an increased prevalence of CD8+ T cells. This was in contrast to a gradual depletion of CD4+ T cells in peripheral blood. The CD8+ IEL were the primary producers of IFN-.gamma. and MIP-1.beta. and were found to retain their potential to produce both IFN-.gamma. and MIP-1.beta. through the entire course of SIV **infection**. SIV-specific **CTL** activity was detected in primary IEL at 1, 2, and 4 wk post-SIV **infection**. These results demonstrated that IEL may be involved in generating antiviral immune responses early in SIV **infection** and in suppressing viral **infection** thereafter. Alterations in homeostasis in epithelia due to severe CD4+ T-cell depletion accompanied by changes in the cytokine and chemokine prodn. by IEL may play a role in the enteropathogenesis of SIV **infection**.

L2 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1998:368321 HCAPLUS
DOCUMENT NUMBER:	129:147947
TITLE:	Characterization of the cutaneous exanthem in macaques infected with a Nef gene variant of SIVmac239
AUTHOR(S):	Sasseville, Vito G.; Rottman, James B.; Du, Zhenjian; Veazey, Ronald; Knight, Heather L.; Caunt, Diane; Desrosiers, Ronald C.; Lackner, Andrew A.
CORPORATE SOURCE:	Division of Comparative Pathology New England Regional Primate Research Center, Harvard Medical School, Southborough, MA, 01772-9102, USA
SOURCE:	Journal of Investigative Dermatology (1998), 110(6), 894-901 CODEN: JIDEAE; ISSN: 0022-202X
PUBLISHER:	Blackwell Science, Inc.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The molecularly cloned viruses known as SIVmac239/R17Y and SIVmac239/YEnef cause extensive lymphocyte activation and induce an acute disease syndrome in macaque monkeys. One manifestation of this syndrome is a severe diffuse cutaneous maculopapular exanthem that is similar to the exanthem assocd. with **HIV-1 infection**. To examine the pathogenesis of this exanthem, biopsies obtained throughout the course of clin. evident rash were examd. for the presence of virus by in situ **hybridization** and immunohistochem., and the cellular infiltrate was characterized with respect to cellular immunophenotype and chemokine receptor expression. The onset of rash was assocd. with abundant simian immunodeficiency virus nucleic acid and protein within perivascular dermal infiltrates and occasionally within intraepithelial cells. Anal. of cellular infiltrates showed that biopsies, obtained on the day of rash onset, were composed of equal nos. of CD4+ and CD8+ lymphocytes and abundant .alpha.E.beta.7 pos. cells surrounding

vessels with upregulated endothelial E-selectin. Moreover, by examg. virus expression in sequential skin biopsies from the same animal, the clearance of virus and the resoln. of rash were assocd. with an increase in the percentage of cells expressing CD8, the chemokine receptor CXCR3, and GMP-17, a marker of cytotoxic granules. These results suggest that activated **cytotoxic T cells** are trafficking to sites of inflammation in the skin and directly or indirectly affect levels of viral replication at these sites.

L2 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:266330 HCAPLUS
DOCUMENT NUMBER: 129:26910
TITLE: Virus-specific CD4+ T cells eliminate Borna disease virus from the brain via induction of cytotoxic CD8+ T cells
AUTHOR(S): Noske, Kerstin; Bilzer, Thomas; Planz, Oliver; Stitz, Lothar
CORPORATE SOURCE: Institut fur Virologie, Justus-Liebig-Universitat Giessen, Germany
SOURCE: Journal of Virology (1998), 72(5), 4387-4395
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Persistent Borna disease virus **infection** of the brain can be prevented by treatment of naive rats with a virus-specific CD4+ T-cell line prior to **infection**. In rats receiving this treatment, only a transient low-level encephalitis was seen compared to an increasingly inflammatory reaction in untreated infected control rats. Virus replication was found in the brain for several days after **infection** before the virus was cleared from the central nervous system. The loss of infectivity from the brain was confirmed by neg. results by reverse transcription-PCR with primers for mRNA, by in situ **hybridization** for both genomic and mRNA, and by immunohistol. Most importantly, in vitro assays revealed that the T-cell line used for transfusion had no cytotoxic capacity. The kinetics of virus clearance were paralleled by the appearance of CD8+ T cells and the expression of perforin in the brain. Testing of lymphocytes isolated from the brains of CD4+ T-cell-treated rats after challenge revealed high cytotoxic activity due to the presence of CD8+ **cytotoxic T cells** at time points when brain lymphocytes from infected control rats induced low-level cytolysis of target cells. Neutralizing antiviral antibodies and gamma interferon were shown not to be involved in the elimination of virus from the brain.

L2 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:267348 HCAPLUS
DOCUMENT NUMBER: 124:314615
TITLE: Major histocompatibility complex class I expression on neurons in subacute sclerosing panencephalitis and experimental subacute measles encephalitis
AUTHOR(S): Gogate, Nitin; Swoveland, Peggy; Yamabe, Toshio; Verma, Lalit; Woyciechowska, Joanna; Tarnowska-Dziduszko, Eugenia; Dymecki, Jerzy; Dhib-Jalbut, Suhayl

CORPORATE SOURCE: Department of Neurology, University of Maryland Hospital, Baltimore, MD, 21201, USA
SOURCE: J. Neuropathol. Exp. Neurol. (1996), 55(4), 435-43
CODEN: JNENAD; ISSN: 0022-3069
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lack of major histocompatibility class I antigens on neurons has been implicated as a possible mechanism for viral persistence in the brain since these antigens are required for **cytotoxic T-lymphocyte** recognition of infected cells. In subacute sclerosing panencephalitis (SSPE), measles virus (MV) persists in neurons, resulting in a fatal chronic **infection**. MHC class I mRNA expression was examd. in formalin-fixed brain tissue from 6 SSPE patients by in situ **hybridization**. In addn. MHC class I protein expression in MV-infected neurons was examd. in exptl. subacute measles encephalitis (SME) by double immunohistochem. MHC class I mRNA expression was upregulated in SSPE tissues studied, and in 5 out of 6 cases the expression was definitively seen on neurons. The percentage of neurons expressing MHC class I mRNA ranged between 20-84% in infected areas. There was no correlation between the degree of **infection** and expression of MHC class I mols. on neurons. Importantly, the no. of neurons co-expressing MHC class I and MV antigens was markedly low, varying between 2-8%. Similar results were obtained in SME where 20-30% of the neurons expressed MHC class I but <8% co-expressed MHC class I and MV antigens. Perivascular infiltrating cells in the infected regions in SME expressed IFN.gamma. immunoreactivity. Thus, MV may not be directly involved in the induction of MHC class I on neurons and cytokines such as IFN.gamma. may play an important role. Furthermore, the paucity of neurons co-expressing MHC class I and MV antigens in SSPE and SME suggests that such cells are either rapidly cleared by **cytotoxic T lymphocytes** (**CTL**), or, alternatively, lack of co-expression of MHC class I on MV infected neurons favors MV persistence in these cells by escaping **CTL** recognition.

L2 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:147170 HCAPLUS
DOCUMENT NUMBER: 124:229727
TITLE: A model of latent adenovirus 5 **infection** in the guinea pig (Cavia porcellus)
AUTHOR(S): Vitalis, Timothy Z.; Keicho, Naoto; Itabashi, Shigeru; Hayashbi, Shizu; Hogg, James C.
CORPORATE SOURCE: St. Paul's Hosp., Univ. British Columbia Pulmonary Res. Lab., Vancouver, BC, Can.
SOURCE: Am. J. Respir. Cell Mol. Biol. (1996), 14(3), 225-31
CODEN: AJRBEL; ISSN: 1044-1549
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A model of adenovirus 5 (Ad5) **infection** was developed in guinea pigs to begin to study its role in the pathogenesis of peripheral lung inflammation. Forty animals were inoculated intranasally with 107.0 pfu of Ad5/animal, and 15 animals inoculated with sterile culture media served as controls. Viral titers were 104.4, 106.1, 105.2, and 102.9 pfu/animal, on days 1, 3, 4, and 7 after **infection**, resp. In situ **hybridization** to

viral DNA and immunocytochem. for Ad5 E1A protein localized the virus to airway and alveolar epithelial cells. Histol. examn. showed an extensive inflammatory cell infiltration around the airways, with epithelial necrosis and an alveolar exudate that caused localized alveolar collapse in the infected areas. Immunocytochem. identified the cells in the infiltrate as **cytotoxic T cells**. Although all animals 20 and 47 days after **infection** had seroconverted to Ad5, virus was not detected in these groups either by viral plaque assay or in situ **hybridization**. Ad5 E1A DNA was detected by polymerase chain reaction in five of six animals 20 days after **infection** and in five of five animals 47 days after **infection**. In these same animals, E1A protein was detected 20 days after **infection** in two and 47 days after **infection** in one while persistent bronchiolitis was obsd. in four and three animals 20 and 47 days after **infection**, resp. These results demonstrate that the guinea pig provides a useful model to study the role of Ad5 **infection** in chronic airway inflammation.

L2 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:381668 HCAPLUS
DOCUMENT NUMBER: 122:158460
TITLE: Mechanism of interleukin 12-mediated toxicities during experimental viral **infections**: role of tumor necrosis factor and glucocorticoids
AUTHOR(S): Orange, Jordan S.; Salazar-Mather, Thais P.; Opal, Steven M.; Spencer, Robert L.; Miller, Andrew H.; McEwen, Bruce S.; Biron, Christine A.
CORPORATE SOURCE: Division of Biology and Medicine, Brown Univ., Providence, RI, 02912, USA
SOURCE: J. Exp. Med. (1995), 181(3), 901-14
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interleukin 12 (IL-12) doses in excess of 100 ng/day have been shown to induce profound immunotoxicities in mice infected with lymphocytic choriomeningitis virus (LCMV). These immunotoxicities are characterized by almost complete inhibition of virus-induced CD8+ T cell expansion and **CTL** activation, and up to 2 log increases in viral replication. They are accompanied by induction of serum tumor necrosis factor (TNF). The studies here were undertaken to characterize mechanisms for the IL-12-induced toxicities and to examine expression and function of TNF in this context. Several physiol. changes were induced in IL-12-treated uninfected and dramatically elevated in IL-12-treated virus-infected mice. IL-12 induced (a) decreases in body wts., >10% in uninfected and >20% in LCMV-infected mice; (b) elevation of circulating glucocorticoid levels to >10 .mu.g/dL in uninfected and >20 .mu.g/dL in infected mice; and (c) decreases in thymic mass, >30% in uninfected and up to 95% in infected mice. These changes are known to be assocd. with circulating TNF. Northern blot and in situ **hybridization** analyses demonstrated that IL-12 induced TNF-.alpha. expression and that LCMV **infection** synergized with IL-12 for induction of this factor. Antibodies neutralizing TNF reversed all of the IL-12-induced toxicities in LCMV-infected mice including the immunotoxicities against CD8+ T cells and

anti-viral defenses. The TNF-mediated immunotoxicities appeared to result from an induced cellular sensitivity to the factor, as splenic leukocytes and CD8+ T cell subsets isolated from LCMV-infected mice were more sensitive to TNF-mediated cytotoxicity in culture than were equiv. populations prepd. from uninfected mice. Expts. with the glucocorticoid type II receptor antagonist, RU486, demonstrated that endogenous glucocorticoids were secondary intermediaries in IL-12-induced thymic atrophy. Studies in IL-2-deficient mice showed that the synergism was dependent upon endogenous IL-2. The results delineate a unique mechanism of TNF-mediated toxicity. They also have implications concerning potential detrimental consequences of in vivo TNF induction and of IL-12 administration for protective anti-viral responses.

L2 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:223910 HCAPLUS
DOCUMENT NUMBER: 122:7884
TITLE: Induction by concanavalin A of specific mRNAs and cytolytic function in a CD8-positive T cell hybridoma
AUTHOR(S): Gu, Jing Jin; Harriss, June V.; Ozato, Keiko; Gottlieb, Paul D.
CORPORATE SOURCE: Dep. Microbiol., Univ. Texas, Austin, TX, 78712, USA
SOURCE: J. Immunol. (1994), 153(10), 4408-17
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A previous report from this lab. described the prodn. of CD8+, class-specific T cell hybridomas which developed specific cytolytic activity and the ability to secrete IL-2 upon Con A or specific Ag stimulation. Unlike normal lymphocytes or long-term **CTL** lines for which exposure to Ag triggers both differentiation and proliferation, T cell hybridoma lines can be activated functionally against a background of continuous proliferation. They therefore provide a unique system with which to study the mol. events involved in the induction of cytolytic function. The expression of mRNA from a series of genes was evaluated by Northern **hybridization** at various times after Con A stimulation of the H-2Ld-specific CD8+ 3D9 hybridoma. Induction of the c-fos proto-oncogene by 45 min poststimulation was followed shortly by c-myc induction. Perforin mRNA was expressed at a low level in the unstimulated hybridomas, but was down-regulated upon Con A stimulation to levels undetectable by PCR. Interestingly, prodn. of granzyme A mRNA was strongly induced by 45 min after Con A stimulation. In the CD8+ RT-1.3G3 hybridoma, which is nonlytic and specific for the **HIV**-1 envelope glycoprotein, c-fos but not granzyme A mRNA was induced by 45 min poststimulation, and no granzyme A mRNA was detectable at any time. Thus, a significant role for granzyme A in the induction of cytolytic activity is suggested. Cytolysis by the 3D9 hybridoma involved both target cell membrane damage and DNA fragmentation, and both Ca2+-dependent and Ca2+-independent cytolysis were obsd. Although TNF-.alpha. mRNA was induced by 4 h poststimulation, Ab to TNF-.alpha. failed to inhibit the Ca2+-independent lysis obsd., leaving the basis for the obsd. Ca2+-independent lysis unexplained.

L2 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:602064 HCAPLUS

DOCUMENT NUMBER: 121:202064
TITLE: Gastric carcinoma: monoclonal epithelial malignant cells expressing Epstein-Barr virus latent **infection** protein
AUTHOR(S): Imai, Shosuke; Koizumi, Shigeki; Sugiura, Makoto; Tokunaga, Masayoshi; Uemura, Yoshiko; Yamamoto, Noriko; Tanaka, Sadao; Sato, Eiichi; Osato, Toyoro
CORPORATE SOURCE: Sch. Med., Hokkaido Univ., Sapporo, 060, Japan
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1994), 91(19), 9131-5
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In 1000 primary gastric carcinomas, 70 (7.0%) contained Epstein-Barr virus (EBV) genomic sequences detected by PCR and Southern blots. The pos. tumors comprised 8 of 9 (89%) undifferentiated lymphoepithelioma-like carcinomas, 27 of 476 (5.7%) poorly differentiated adenocarcinomas, and 35 of 515 (6.8%) moderately to well-differentiated adenocarcinomas. In situ EBV-encoded small RNA 1 **hybridization** and hematoxylin/eosin staining in adjacent sections showed that the EBV was present in every carcinoma cell but was not significantly present in lymphoid stroma and in normal mucosa. Two-color immunofluorescence and hematoxylin/eosin staining in parallel sections revealed that every keratin-pos. epithelial malignant cell expressed EBV-detd. nuclear antigen 1 (EBNA1) but did not significantly express CD45+ infiltrating leukocytes. A single fused terminal fragment was detected in each of the EBNA1-expressing tumors, thereby suggesting that the EBV-carrying gastric carcinomas represent clonal proliferation of cells infected with EBV. The carcinoma cells had exclusively EBNA1 but not EBNA2, -3A, -3B, and -3C; leader protein; and latent membrane protein 1. The patients with EBV-carrying gastric carcinoma had elevated serum EBV-specific antibodies. The EBV-specific cellular immunity was not significantly reduced; however, the **cytotoxic T-cell** target antigens were not expressed. These findings strongly suggest a causal relation between a significant proportion of gastric carcinoma and EBV, and the virus-carrying carcinoma cells may evade immune surveillance.

L2 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:252437 HCAPLUS
DOCUMENT NUMBER: 118:252437
TITLE: Interferon-inducible gene expression in chimpanzee liver infected with hepatitis C virus
AUTHOR(S): Kato, Tamami; Esumi, Mariko; Yamashita, Susumu; Abe, Kenji; Shikata, Toshio
CORPORATE SOURCE: Sch. Med., Nihon Univ., Tokyo, 173, Japan
SOURCE: Virology (1992), 190(2), 856-60
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mol. host response to hepatitis C virus (HCV) **infection** was examd. by isolation of HCV-induced genes from a cDNA library constructed from chimpanzee liver during the acute phase of hepatitis C. Two cDNA clones, 130-7 and 130-51, were obtained by differential **hybridization** with cDNA probes prepd. from poly(A)+ RNAs of infected and uninfected livers. Northern blot

anal. revealed that the 130-7 and 130-51 cDNAs were expressed as 1.5- and 1.0-kb products, resp., in chimpanzee liver and that the induction rates of the two were 20 and 4, resp. Nucleotide sequence analyses of these cDNA inserts showed that the sequence of cDNA 130-7 was that of a class I major histocompatibility antigen and that the sequence of cDNA 130-51 was 98% homologous with a human interferon-inducible mRNA. These results suggest that HCV **infection** may actively induce interferon, which in turn induces the expressions of these interferon-inducible genes. Furthermore, the high expression of HLA class I antigen in the acute phase of hepatitis C suggests that liver cell injury in HCV **infection** may be mediated by **cytotoxic T cells** that recognize viral antigen in assocn. with HLA class I antigen.

L2 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:100253 HCAPLUS
DOCUMENT NUMBER: 118:100253
TITLE: Epstein-Barr virus and Hodgkin's disease: Transcriptional analysis of virus latency in the malignant cells
AUTHOR(S): Deacon, E. M.; Pallesen, G.; Niedobitek, G.; Crocker, J.; Brooks, L.; Rickinson, A. B.; Young, L. S.
CORPORATE SOURCE: Med. Sch., Univ. Birmingham, Birmingham, B15 2TJ, UK
SOURCE: J. Exp. Med. (1993), 177(2), 339-49
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Epstein-Barr virus (EBV) is assocd. with a no. of different human tumors and appears to play different pathogenetic roles in each case. Thus, immunoblastic B cell lymphomas of the immunosuppressed display the full pattern of EBV latent gene expression (expressing Epstein-Barr nuclear antigen [EBNA]1, 2, 3A, 3B, 3C, and -LP, and latent membrane protein [LMP]1, 2A, and 2B), just as do B lymphoblastoid cell lines transformed by the virus in vitro. In contrast, those EBV-assocd. tumors with a more complex, multistep pathogenesis show more restricted patterns of viral gene expression, limited in Burkitt's lymphoma to EBNA1 only and in nasopharyngeal carcinoma (NPC) to EBNA1 and LMP1, 2A, and 2B. Recent evidence has implicated EBV in the pathogenesis of another lymphoid tumor, Hodgkin's disease (HD), where the malignant Hodgkin's and Reed-Sternberg (HRS) cells are EBV genome pos. in up to 50% of cases. Here preliminary results are extended on viral gene expression in HRS cells by adopting polymerase chain reaction-based and in situ **hybridization** assays capable of detecting specific EBV latent transcripts diagnostic of the different possible forms of EBV latency. The transcriptional program of the virus in HRS cells is similar to that seen in NPC in several respects: (a) selective expression of EBNA1 mRNA from the BamHI F promoter: (b) downregulation of the BamHI C and W promoters and their assocd. EBNA mRNAs; (c) expression of LMP1 and, in most cases, LMP2A and 2B transcripts; and (d) expression of the rightward-running BamHI A transcripts once thought to be unique to NPC. This form of latency, consistently detected in EBV-pos. HD irresp. of histol. subtype, implies an active role for the virus in the pathogenesis of HD and also suggests that the tumor may remain sensitive to at least

certain facets of the EBV-induced **cytotoxic T cell** response.

L2 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:19650 HCAPLUS
DOCUMENT NUMBER: 116:19650
TITLE: Intracellular antigen found in subpopulation of CD8+ T-lymphocytes and monoclonal antibody reactive with same
INVENTOR(S): Anderson, Paul J.; Streuli, Michel; Schlossman, Stuart F.
PATENT ASSIGNEE(S): Dana-Farber Cancer Institute, USA
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 436400	A1	19910710	EP 1990-314456	19901231
EP 436400	B1	19990825		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5079343	A	19920107	US 1990-460678	19900105
JP 05184387	A2	19930727	JP 1990-415435	19901228
AT 183777	E	19990915	AT 1990-314456	19901231
CA 2033644	AA	19910706	CA 1991-2033644	19910104

PRIORITY APPLN. INFO.: US 1990-460678 19900105

AB A 15-kilodalton (kd) protein antigen (TIA-1 antigen) is assocd. with cytoplasmic granules in cytolytic T-lymphocytes and natural killer cells. Monoclonal antibodies immunol. reactive with TIA-1 antigen, and nucleic acid probes encoding polypeptides that are immunol. cross-reactive with TIA-1 antigen, can be used to identify cytolytic lymphocytes in a sample and provide early warning of **infections**. Thus, mice were immunized with digitonin-permeabilized T-lymphocytes, and their splenocytes were subsequently fused with NS-1 myeloma cells. The hybridoma cells were cloned and screened with permeabilized T-lymphocytes by flow cytometry. TIA-1 antigen was expressed by 55% of CD8+ cells and 6% of CD4+ cells, but not by immortalized T-cell lines or by B-cells. TIA-1 antigen did not have serine protease activity. A .lambda. gt11 cDNA library, prepd. from RNA isolated from a **cytotoxic T-cell** clone, was subjected to immunoscreening using TIA-1, and a cloned recombinant cDNA encoding the TIA-1 antigen was sequenced.

L2 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:512596 HCAPLUS
DOCUMENT NUMBER: 115:112596
TITLE: Mutational analysis of regulation of MHC and antiviral genes
AUTHOR(S): Rodgers, John R.; Wyde, Philip R.; Rich, Robert R.
CORPORATE SOURCE: Dep. Immunol. Microbiol., Baylor Coll. Med., Houston, TX, 77030, USA
SOURCE: J. Immunol. (1991), 146(6), 1979-86
CODEN: JOIMA3; ISSN: 0022-1767

DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Cytotoxic T-lymphocyte** mediated selection for loss of expression of Mta by H-2-heterozygous SV40-transformed mouse fibroblasts (line 24SV) produced an unusual phenotypic class of maternally transmitted antigen (Ag) neg. mutants defective in both MHC expression and in anti-viral activity. Severely reduced surface expression of class I MHC Ag from multiple loci of both haplotypes correlated with low levels of MHC H chain and .beta.2-microglobulin mRNA. Inasmuch as IFN can up-regulate class I expression and some fibroblasts elaborate autocrine IFN-.beta., the authors examd. whether IFN could restore wild-type expression of class I MHC Ag. However, IFN could not restore wild-type expression. Moreover, the fold-increases in class I Ag and mRNA expression were significantly reduced in mutant cells compared to wild-type cells. These results suggested that the mutants might have generalized defects in IFN response. Inasmuch as the induction of an anti-viral state is a hallmark of IFN responses, the authors exposed cells to IFN-.alpha., -.beta., or -.gamma. and challenged with virus. 24SV cells, exposed to any of the three IFNs, were completely protected from destruction by vesicular stomatitis, mengovirus or respiratory syncytial viruses. In contrast, MHC and anti-viral defective mutants could not be protected from virus-induced lysis by any IFN. Somatic cell **hybridization** analyses indicated that both basal MHC and IFN-inducible phenotypes were recessive to wild-type, and that a trans-acting regulatory factor required for basal MHC expression is defectively expressed in the mutants. Such a factor may integrate the organismal response to virus **infection**, encompassing both immune and nonimmune anti-viral responses.

L2 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:512529 HCAPLUS
DOCUMENT NUMBER: 115:112529
TITLE: The role of CD4+ cells in sustaining lymphocyte proliferation during lymphocytic choriomeningitis virus **infection**
AUTHOR(S): Kasaian, Marion T.; Leite-Morris, Kimberly A.; Biron, Christine A.
CORPORATE SOURCE: Div. Biol. Med., Brown Univ., Providence, RI, 02912, USA
SOURCE: J. Immunol. (1991), 146(6), 1955-63
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The murine immune response to lymphocytic choriomeningitis virus [LCMV] **infection** involves the activation of CD8+, class I MHC-restricted and virus-specific **CTL**. At times coinciding with **CTL** activation, high levels of IL-2 gene expression and prodn. occur, the IL-2R is expressed, and T cell blastogenesis and proliferation are induced. Although both CD4+ and CD8+ T cell subsets transcribe IL-2, the CD4+ subset appears to be the major producer of IL-2 whereas the CD8+ subset appears to be the major proliferating population when the subsets are sepd. after activation in vivo. The studies presented here were undertaken to examine the contribution made by the CD4+ subset to lymphocyte proliferation in vivo. Responses to LCMV **infection** were examd. in intact mice and in mice depleted of CD4+ or CD8+ subsets

by antibody treatments in vivo. Protocols were such that in vivo treatments with anti-CD4 or anti-CD8 depleted the resp. subset by >90%. In situ **hybridizations** demonstrated that the IL-2 gene was expressed in non-B lymphocytes isolated from either CD4+ cell-depleted or CD8+ cell-depleted mice on day 7 post-**infection** with LCMV. When placed in culture, however, cells from CD8+ cell-depleted mice produced higher levels of detectable IL-2 than did cells isolated from CD4+ cell-depleted mice on day 7 post-**infection**. IL-2 was apparently produced in vivo in mice depleted of either CD4+ or CD8+ cells, as expression of the gene for the p55 chain of the IL-2R, IL-2 responsiveness, and lymphocyte proliferation were obsd. with cells isolated from both sets of mice. Lymphocyte proliferation was shown to be sustained in mice depleted of CD4+ cells in vivo by three criteria: 1) non-B lymphocytes isolated from infected mice depleted of CD4+ cells underwent more DNA synthesis than did those isolated from uninfected mice or from infected mice depleted of CD8+ cells; 2) leukocyte yields were expanded during **infection** of CD4+ cell-depleted mice; and 3) CD8+ cell nos. were increased during **infection** of CD4+ cell-depleted mice. The majority of non-B lymphocytes having the characteristics of blast lymphocytes was recovered in the CD8+ populations isolated from infected CD4+ cell-depleted mice. These finding suggest that the requirement for the CD4+ subset to sustain CD8+ lymphocyte proliferation in vivo is limited, and that CD4+ and CD8+ cell types can function independently in many aspects of their responses to viral **infections**.

L2 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:151425 HCAPLUS
DOCUMENT NUMBER: 112:151425
TITLE: Effects of cyclosporin A on IL-2 production and lymphocyte proliferation during **infection** of mice with lymphocytic choriomeningitis virus
AUTHOR(S): Kasaian, Marion T.; Biron, Christine A.
CORPORATE SOURCE: Div. Biol. Med., Brown Univ., Providence, RI, 02912, USA
SOURCE: J. Immunol. (1990), 144(1), 299-306
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The immunosuppressive agent, cyclosporin A (CsA) blocks prodn. of IL-2 by lymphocytes in vitro, and impairs immune responses in vivo. During **infection** of mice with lymphocytic choriomeningitis virus (LCMV), IL-2 is produced by spleen lymphocytes with a time course corresponding to that of T cell activation and proliferation, but distinct from NK cell activation and proliferation. To evaluate the requirement for IL-2 in supporting lymphocyte proliferation in vivo, and to investigate the mechanisms of CsA-induced immunosuppression, the effects of CsA on LCMV-elicited responses were examd. CsA had profound effects on lymphocyte expansion and **CTL** activation on day 7 postinfection, the peak of the T cell response to LCMV. Proliferation of both the CD4+ and CD8+ T cell subsets was affected. Inhibition of T cell expansion was accompanied by the inhibition of IL-2 prodn. and IL-2 responsiveness. In situ **hybridization** revealed a 50% redn. in the percentage of cells transcribing IL-2, suggesting that

CsA blocked IL-2 prodn. at the level of gene transcription. Transcripts of the gene for the IL-2R p55 chain are also normally elevated during **infection**, and CsA treatment resulted in an 80% redn. in the percentage of cells transcribing this gene. A reduced responsiveness of freshly isolated cells to rIL-2 in vitro correlated with the redn. of IL-2 receptor gene transcription pos. cells. In contrast to effects of the drug on T cells, the level of NK cell activation was not decreased as a result of CsA treatment. These observations suggest that the IL-2 produced by lymphocytes in vivo in response to virus **infection** is required to promote the T cell response to LCMV, but do not support a role for IL-2 in NK cell activation under the conditions examd. Furthermore, the data demonstrate the profound inhibition of lymphocyte proliferation induced by CsA treatment during an in vivo immune response.

L2 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:592901 HCAPLUS
DOCUMENT NUMBER: 111:192901
TITLE: Detection of perforin and granzyme A mRNA in infiltrating cells during **infection** of mice with lymphocytic choriomeningitis virus
AUTHOR(S): Mueller, Christoph; Kaegi, David; Aebischer, Toni; Odermatt, Bernhard; Held, Werner; Podack, Eckhard R.; Zinkernagel, Rolf M.; Hengartner, Hans
CORPORATE SOURCE: Dep. Pathol., Univ. Bern, Bern, Switz.
SOURCE: Eur. J. Immunol. (1989), 19(7), 1253-9
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The anal. of gene expression in **cytotoxic T cells** by in situ **hybridization** of serial liver and brain sections from mice infected with lymphocytic choriomeningitis virus (LCMV) and immunostaining with T cell marker- and virus-specific antibodies revealed a close histol. assocn. of infiltrating lymphocytes expressing the perforin and granzyme A genes with virally infected cells. Maximal frequency of perforin and granzyme A mRNA-contg. cells on liver sections preceded by about 2 days maximal LCMV-specific cytotoxicity of the lymphoid liver infiltrating cells. These results are most consistent with an involvement of perforin and granzyme A in cell-mediated cytotoxicity in vivo.

L2 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:628438 HCAPLUS
DOCUMENT NUMBER: 109:228438
TITLE: Immunization with solid matrix-antibody-antigen complexes containing surface or internal virus structural proteins protects mice from **infection** with the paramyxovirus, simian virus 5
AUTHOR(S): Randall, R. E.; Young, D. F.; Southern, J. A.
CORPORATE SOURCE: Dep. Biochem. Microbiol., Univ. St. Andrews, St. Andrews/Fife, KY16 9AL, UK
SOURCE: J. Gen. Virol. (1988), 69(10), 2517-26
CODEN: JGVIAY; ISSN: 0022-1317
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A mouse model system was developed to examine the ability of purified virus proteins to protect mice from **infection** with the paramyxovirus simian virus 5. The system is based on the **infection** of mouse lungs by intranasal administration of **infectious** virus. The relative amts. of virus proteins and nucleic acid present within infected lungs were estd. either by Western blot anal. of disrupted lung tissues or by in situ **hybridization** studies using cryostat sections of infected lungs. During a normal time course of **infection** in non-immunized mice increasing amts. of virus protein and nucleic acid were detected in the lungs until 3 days post-**infection** (p.i.). Thereafter the amt. of virus present within the lungs remained relatively const. until 7 days p.i. when there was a rapid decrease. **Cytotoxic T cells**, but not neutralizing antibody, could be detected at the time when the amt. of virus within the lungs was decreasing. Prior immunization of mice with solid matrix-antibody-antigen (SMAA) complexes contg. either surface or internal virus structural proteins reduced the amt. of virus replication within infected lungs, the greatest degree of protection being obsd. when nucleoprotein or matrix protein was used to immunize the mice. There was no correlation between the degree of protection obsd. and the level of neutralizing antibody present in immunized animals; no neutralizing antibody was detected in mice immunized with internal virus proteins even at the time of sacrifice 5 days p.i. It was previously shown that immunization of mice with SMAA complexes contg. either surface or internal virus structural proteins can induce **cytotoxic T cells** so the most likely explanation for the protection obsd. in immunized mice is through the induction of **cytotoxic T cells**.

L2 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:174274 HCAPLUS
DOCUMENT NUMBER: 106:174274
TITLE: Epstein-Barr virus-specific T-cell recognition of B-cell transformants expressing different EBNA 2 antigens
AUTHOR(S): Wallace, L. E.; Young, L. S.; Rowe, M.; Rowe, D.; Rickinson, A. B.
CORPORATE SOURCE: Med. Sch., Univ. Birmingham, Birmingham, B15 2TJ, UK
SOURCE: Int. J. Cancer (1987), 39(3), 373-9
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Epstein-Barr (EB) virus isolates can be classified as type A or type B depending upon the identity of the virus-encoded nuclear antigen EBNA 2. The EBNA 2A and 2B proteins show limited amino-acid homol. and induce largely non-cross-reactive antibody responses in humans. To examine whether EBNA 2 might also be a target for virus-specific **cytotoxic T-cell** responses (like intracellular antigens in other viral systems), normal B cells from non-immune donors of known HLA type were transformed in vitro with virus isolates either of type A (from the B95-8 and IARC-BL74 cell lines) or of type B (from the AG876 and IARC-BL16 cell lines) to provide a suitable panel of target cells. DNA **hybridization** with type-specific probes and immunoblotting with type-specific antisera confirmed the EBNA 2 type of the resident virus in the

various in vitro transformants. These cells were then tested as targets for virus-specific **cytotoxic T cells**, the latter being prepd. from type-A virus-infected donors by in vitro reactivation of memory cells from peripheral blood using autologous type-A virus-transformed cells as stimulators. Such effector cells lysed type-A virus-transformed and type-B virus-transformed target cells equally well, indicating that EBNA 2 (in particular that part of the protein which varies between virus types) seems not to be a dominant antigen for the induction of EB virus-specific cytotoxic responses.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 10:41:30 ON 17 JUN 2002)

L3	296	SEA ABB=ON PLU=ON L2
L4	170	SEA ABB=ON PLU=ON L3 AND ANTIGEN?
L5	119	DUP REM L4 (51 DUPLICATES REMOVED)
L6	65	SEA ABB=ON PLU=ON L5 AND (DETERM? OR IDENTIF? OR SCREEN? OR DETECT? OR DET##)
L7	18	SEA ABB=ON PLU=ON L6 AND (TREAT? OR THERAP?)
L8	46	SEA ABB=ON PLU=ON L6 AND (GENE OR GENETIC)
L9	1	SEA ABB=ON PLU=ON L6 AND (MICROARRAY? OR MICRO ARRAY?)
L10	53	SEA ABB=ON PLU=ON L7 OR L8 OR L9

L10 ANSWER 1 OF 53 MEDLINE

ACCESSION NUMBER:	2002044832 MEDLINE
DOCUMENT NUMBER:	21628502 PubMed ID: 11756778
TITLE:	Aggressive Epstein-Barr virus-associated, CD8+, CD30+, CD56+, surface CD3-, natural killer (NK)-like **cytotoxic T-cell** lymphoma.
AUTHOR:	Tao Jianguo; Shelat Suresh G; Jaffe Elaine S; Bagg Adam
CORPORATE SOURCE:	Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, Pennsylvania 19104, USA.
SOURCE:	AMERICAN JOURNAL OF SURGICAL PATHOLOGY, (2002 Jan) 26 (1) 111-8. Journal code: 7707904. ISSN: 0147-5185.
PUB. COUNTRY:	United States
	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200201
ENTRY DATE:	Entered STN: 20020124
	Last Updated on STN: 20020125
	Entered Medline: 20020117

AB We report an unusual case of aggressive natural killer (NK)-like **cytotoxic T-cell** lymphoma in a previously healthy immunocompetent West African male. He presented with a fever of unknown origin, subsequently developed erythematous skin nodules, generalized lymphadenopathy, and hepatosplenomegaly, and then died of multiple organ failure. A skin nodule and lymph node biopsy showed an infiltrate of pleomorphic atypical medium and large lymphoid cells with extensive necrosis and prominent apoptosis. Peripheral blood and ascites also harbored these cells, with cytology revealing irregular nuclear folding and basophilic cytoplasm, and some with azurophilic cytoplasmic granules. Flow

cytometry and immunohistochemistry demonstrated the expression of CD2, CD7, CD8, CD30, CD56, and cytoplasmic but not surface CD3. In situ **hybridization** demonstrated Epstein-Barr virus transcripts. A monoclonal T-cell receptor gamma chain **gene** rearrangement was **detected** by polymerase chain reaction. This is the first reported case of an NK-like T-cell lymphoma with these unusual features, making precise classification difficult. Some features suggest an NK1.1 or NKT lymphocyte origin. Because the earliest clinical manifestation was splenomegaly and abnormal liver function, the normal cellular counterpart may be a distinct subset of NK1.1 cells normally present in hepatosplenic sinusoids. This tumor disseminated early and pursued a fulminant clinical course, thus emphasizing the importance of early recognition and diagnosis.

L10 ANSWER 2 OF 53 MEDLINE
ACCESSION NUMBER: 2001319289 MEDLINE
DOCUMENT NUMBER: 21286250 PubMed ID: 11391627
TITLE: Expression of human tumor-associated **antigen** RCAS1 in Reed-Sternberg cells in association with Epstein-Barr virus **infection**: a potential mechanism of immune evasion.
AUTHOR: Ohshima K; Muta K; Nakashima M; Haraoka S; Tutiya T; Suzumiya J; Kawasaki C; Watanabe T; Kikuchi M
CORPORATE SOURCE: Department of Pathology, School of Medicine, Fukuoka University, Fukuoka, Japan.. ohshima@fukuoka-u.ac.jp
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (2001 Jul 1) 93 (1) 91-6.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

AB RCAS1 (receptor-binding cancer **antigen** expressed on SiSo cells) is present in neoplastic cells, induces apoptosis of natural killer (NK)/T cells and plays a role in immune evasion. Fas ligand (FasL) is considered to have similar roles. The Epstein-Barr virus (EBV)-encoded latent membrane protein is expressed by malignant Hodgkin and Reed-Sternberg (H&RS) cells of EBV-associated Hodgkin's disease (HD) and considered to be a target of **cytotoxic T lymphocytes** (**CTLs**). However, **CTL** response is inadequate in HD. To **determine** whether RCAS1 and FasL are expressed in EBV-associated HD and participate in immune evasion, tissues of 20 EBV(-) and 15 EBV(+) HD cases were immunohistochemically stained for RCAS1, FasL and HLA classes I and II, whose deficiencies could explain **CTL** escape. Lymphocytes surrounding H&RS cells tended to be CD4(+) cells and rarely CD8(+), TIA-1(+) (cytotoxic marker) or NK cells. HLA class I and/or II were expressed in all EBV(+) HD cases, and RCAS1-expressing H&RS cells were found in 14/15 (93%) EBV(+) HD cases but only 8/20 (40%) EBV(-) HD cases ($p < 0.05$). FasL was **detected** in 9/15 (60%) and 7/20 (35%) EBV(+) and EBV(-) HD cases, respectively. ssDNA-positive (apoptotic) lymphocytes, surrounding H&RS cells, were rarely seen but were present in RCAS1(+) cases (20/22 cases, 91%) rather than negative cases (0/13

cases, 0%) ($p < 0.005$). Our findings suggest that EBV(+) H&RS cells might evade the host immune response by expressing RCAS1 rather than FasL.

L10 ANSWER 3 OF 53 MEDLINE
ACCESSION NUMBER: 2000416875 MEDLINE
DOCUMENT NUMBER: 20384126 PubMed ID: 10926739
TITLE: gamma delta T-cell lymphoma of the skin: a clinical, microscopic, and molecular study.
COMMENT: Comment in: Arch Dermatol. 2000 Aug;136(8):1052-4
AUTHOR: Toro J R; Beaty M; Sorbara L; Turner M L; White J; Kingma D W; Raffeld M; Jaffe E S
CORPORATE SOURCE: Dermatology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892-1908, USA.. torojo@exchange.nih.gov
SOURCE: ARCHIVES OF DERMATOLOGY, (2000 Aug) 136 (8) 1024-32. Ref: 42
Journal code: 0372433. ISSN: 0003-987X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW OF REPORTED CASES)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000907
Last Updated on STN: 20020313
Entered Medline: 20000828

AB BACKGROUND: Only a few cases of primary gamma delta cutaneous T-cell lymphoma (CTCL) have been reported. We encountered 3 cases of this rare condition. OBJECTIVES: To characterize gamma delta CTCL by clinical, microscopic, and molecular methods and to investigate the role of Epstein-Barr virus (EBV) **infection** in its pathogenesis. DESIGN: Patients were evaluated by clinical examination, and biopsy specimens of lesional skin were examined by light microscopy and immunohistochemistry. Polymerase chain reaction amplification for T-cell receptor gamma **gene** rearrangements and in situ **hybridization** for EBV were performed on 3 biopsy specimens. SETTING: National Institutes of Health, a tertiary referral center. PATIENTS: Individuals with a clinical and histologic diagnosis of primary gamma delta CTCL. OUTCOME MEASURES: Clinical, light microscopic, and immunohistochemical features, and the presence of T-cell rearrangement and EBV RNA in biopsy specimens. RESULTS: Patients exhibited multiple plaques, tumors, and/or subcutaneous nodules primarily distributed over the extremities. Individuals exhibited an aggressive clinical course with resistance to multiagent chemotherapy and radiation. Microscopic examination revealed epidermotropism in 2 cases, a dermal infiltrate in all 3 cases, and subcutaneous involvement in 1 case. Immunohistochemical studies showed the presence of CD3(+)TCR delta(+) in 3 patients, CD8(+)in 1, and CD4(+), CD20(+), CD56(+), and beta F1(+) in none. All 3 cases exhibited an activated **cytotoxic T-cell** phenotype positive for T-cell intracellular **antigen** 1, perforin, and granzyme B. A clonal T-cell receptor gamma chain **gene** rearrangement was **detected** in all 3 cases by polymerase chain reaction. In situ **hybridization** was

negative for EBV sequences in all 3 cases. CONCLUSION: gamma delta Cutaneous T-cell lymphomas are EBV-negative lymphomas that express a mature cytotoxic phenotype and have an aggressive clinical behavior. Arch Dermatol. 2000;136:1024-1032

L10 ANSWER 4 OF 53 MEDLINE
ACCESSION NUMBER: 2000396117 MEDLINE
DOCUMENT NUMBER: 20320824 PubMed ID: 10861473
TITLE: Low frequency of HLA-A*0201 allele in patients with Epstein-Barr virus-positive nasal lymphomas with polymorphic reticulosis morphology.
AUTHOR: Kanno H; Kojya S; Li T; Ohsawa M; Nakatsuka S; Miyaguchi M; Harabuchi Y; Aozasa K
CORPORATE SOURCE: Department of Pathology, Osaka University Graduate School of Medicine, Suita, Osaka, Japan.
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (2000 Jul 15) 87 (2) 195-9.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000816

AB Lymphoproliferative diseases of the nasal cavity and paranasal sinuses occur frequently in Asian countries and are histologically categorized as monomorphic ordinary lymphoma and polymorphic reticulosis (PR) with apparent inflammatory cell infiltration. The large atypical cells in PR show natural-killer cell nature and frequently contain Epstein-Barr virus (EBV) DNA. Among the EBV **genes** involved in latent **infection**, those encoding EBV latent membrane proteins are frequently expressed in PR. Several **cytotoxic T-lymphocyte** (**CTL**) defined epitopes have been mapped to latent membrane proteins restricted with HLA-A2, -A11 or -A24 **antigens**. Thus, the HLA-A allele may affect the development of PR. To examine this possibility, HLA-A alleles of 25 patients with EBV(+) PR were **determined** with low-resolution polymerase chain reaction-based typing using HLA-A locus sequence-specific primer combinations. The frequency of HLA-A alleles including HLA-A2 and -A24 **antigens** in PR patients was lower than that in the normal Japanese population, but the difference was not significant. Since HLA-A2-restricted **CTL** responses are well delineated at the A2-subtype level, the A2-subtype of PR cases with HLA-A2 **antigen** was further **determined** by high-resolution **genetic** typing. The frequency of HLA-A*0201 in PR was significantly lower than in the normal population (p=0.0314). The HLA-A*0201-restricted **CTL** responses may thus function in vivo to suppress the development of overt lymphoma.

L10 ANSWER 5 OF 53 MEDLINE
ACCESSION NUMBER: 2000273932 MEDLINE
DOCUMENT NUMBER: 20273932 PubMed ID: 10811848
TITLE: **HIV**-specific **cytotoxic T lymphocytes** traffic to lymph nodes and

localize at sites of **HIV** replication and cell death.

COMMENT: Comment in: J Clin Invest. 2000 May;105(10):1333-4

AUTHOR: Brodie S J; Patterson B K; Lewinsohn D A; Diem K; Spach D; Greenberg P D; Riddell S R; Corey L

CORPORATE SOURCE: Department of Laboratory Medicine, University of Washington, Seattle, Washington 98195, USA.. sjbrodie@u.washington.edu

CONTRACT NUMBER: AI-30731 (NIAID)
AI-36613 (NIAID)
AI-41535 (NIAID)
+

SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (2000 May) 105 (10) 1407-17.
Journal code: 7802877. ISSN: 0021-9738.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS

ENTRY MONTH: 200006

ENTRY DATE: Entered STN: 20000622
Last Updated on STN: 20000622
Entered Medline: 20000612

AB We have tracked the in vivo migration and have **identified** in vivo correlates of **cytotoxic T-lymphocyte** (**CTL**) activity in **HIV**-seropositive subjects infused with autologous **gene**-marked CD8(+) **HIV**-specific **CTL**. The number of circulating **gene**-marked **CTL** ranged from 1.6 to 3.5% shortly after infusion to less than 0.5% 2 weeks later. **Gene**-marked **CTL** were present in the lymph node at 4.5- to 11-fold excess and colocalized within parafollicular regions of the lymph node adjacent to cells expressing **HIV** tat fusion transcripts, a correlate of virus replication. The **CTL** clones expressed the CCR5 receptor and localized among **HIV**-infected cells expressing the ligands MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of virus replication. Aggregates of apoptotic cells and cells expressing granzyme-B localized within these same sites. In contrast, lymph node sections from untreated **HIV**-seropositive subjects, all with significant viral burden (> 50,000 **HIV** RNA copies/mL plasma), showed no CC-chemokine expression and exhibited only sporadic and randomly distributed cells expressing granzymes and/or apoptotic cells. These studies show that the infused **CTL** specifically migrate to sites of **HIV** replication and retain their **antigen**-specific cytolytic potential. Moreover, these studies provide a methodology that will facilitate studies of both the magnitude and functional phenotype of Ag-specific CD8(+) T cells in vivo.

L10 ANSWER 6 OF 53 MEDLINE

ACCESSION NUMBER: 2000138103 MEDLINE

DOCUMENT NUMBER: 20138103 PubMed ID: 10672057

TITLE: Hepatosplenic gammadelta T-cell lymphoma: relation to Epstein-Barr virus and activated cytotoxic molecules.

AUTHOR: Ohshima K; Haraoka S; Harada N; Kamimura T; Suzumiya J; Kanda M; Kawasaki C; Sugihara M; Kikuchi M

CORPORATE SOURCE: Department of Pathology, School of Medicine, Fukuoka University, Kyushu University, Fukuoka, Japan.
SOURCE: HISTOPATHOLOGY, (2000 Feb) 36 (2) 127-35.
Journal code: 7704136. ISSN: 0309-0167.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000317

AB AIMS: Hepatosplenic gammadelta T-cell lymphoma (TCL) is a rare, aggressive subset of peripheral TCL that presents with hepatosplenomegaly and cytopenia. Epstein-Barr virus (EBV) **infection** and activated cytotoxic molecules (granzyme and perforin) are uncommon in hepatosplenic gammadelta **CTL**. EBV **infection** and activated cytotoxic molecules are occasionally **detected** in non-hepatosplenic gammadelta TCL. We describe the clinicopathological features of three Japanese cases who were not immunodeficient. METHODS AND RESULTS: All cases showed gammadelta T-cell type (CD2+, CD3+, T-cell receptor (TCR)delta-1+, betaF1-). Two cases expressed natural killer (NK) cell-associated **antigens** (CD8-, CD16+, CD56+; CD8-, CD16-, CD56+), and one expressed CD8 (CD8+, CD16-, CD56-). All cases expressed cytotoxicity-associated molecules (perforin, granzyme B, TIA-1 and Fas ligand). However, perforin and Fas ligand were not **detected** in one case. In-situ **hybridization** analysis with EBER probes revealed strong nuclear positivity in all neoplastic cells. In addition, two cases showed clonal bands of the EBV terminal repeat (TR) **gene**. Cytologically, instead of the presence of monomorphic medium-sized cells, our three cases showed pleomorphic medium-sized and large cells. CONCLUSIONS: Our gammadelta TCL cases were clinicopathologically considered to be compatible with hepatosplenic gammadelta T-cell lymphoma. However, with regard to EBV association, activated cytotoxic profile and cytological features they resembled non-hepatosplenic gammadelta TCL. EBV may play a role in this disease by inducing cellular activation.

L10 ANSWER 7 OF 53 MEDLINE
ACCESSION NUMBER: 2000067413 MEDLINE
DOCUMENT NUMBER: 20067413 PubMed ID: 10599306
TITLE: Clinical, immunohistochemical and phenotypic features of aggressive nodal cytotoxic lymphomas, including alpha/beta, gamma/delta T-cell and natural killer cell types.
AUTHOR: Ohshima K; Suzumiya J; Sugihara M; Kanda M; Shimazaki K; Kawasaki C; Haraoka S; Kikuchi M
CORPORATE SOURCE: Department of Pathology, School of Medicine, Fukuoka University, Japan.
SOURCE: VIRCHOWS ARCHIV, (1999 Aug) 435 (2) 92-100.
Journal code: 9423843. ISSN: 0945-6317.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 200001

ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000106

AB Cytotoxic cells include natural killer (NK) cells and cytotoxic alpha beta and gamma delta T lymphocytes (**CTLs**). These cells express cytotoxic molecules of T-cell restricted intracellular **antigen** (TIA-1), and activated cytotoxic molecules of perforin, granzyme B, and FasL. Recent studies suggest that most extranodal T-cell lymphomas are derived from **CTLs**, and that NK cell lymphomas are extranodal. However, only a few nodal NK and cytotoxic lymphomas have been described so far. We present here the clinicopathological features of seven cases of nodal cytotoxic T and NK cell lymphomas. The study excluded anaplastic large-cell lymphomas expressing cytotoxic molecules. The neoplastic cells of all cases contained activated cytotoxic molecules of TIA-1, granzyme B, Fas ligand, and/or perforin. Phenotypically and genotypically, four cases showed alpha beta T cell type [CD2+, CD3+, T-cell receptor (TCR)-delta-1-, beta F1+, and TCR **gene** rearrangement], two cases showed gamma delta cell type [CD2+, CD3+, T-cell receptor (TCR) delta-1+, beta F1-, and TCR **gene** rearrangement], and one case showed NK cell type [CD2+, CD3-, CD56+, T-cell receptor (TCR) delta-1-, beta F1-, and TCR **gene** germline]. Using Southern blot analysis, Epstein-Barr virus (EBV) sequences were **detected** in six cases, and monoclonal terminal repeat proliferation was confirmed. In addition, in situ **hybridization** (ISH) studies for EBV showed EBV **infection** in almost all neoplastic cells. Clinically, all patients presented with peripheral lymphadenopathy in high clinical stages and showed an aggressive course. Hepatosplenomegaly was **detected** in six cases. During the course of the disease, bone marrow and extranodal invasion were noted in five cases. The nodal type showed an aggressive clinical course in all cases but one, as did the extranodal type. The nodal type varied in phenotype, but was closely associated with EBV **infection**.

L10 ANSWER 8 OF 53 MEDLINE
ACCESSION NUMBER: 2000060861 MEDLINE
DOCUMENT NUMBER: 20060861 PubMed ID: 10595412
TITLE: Molecular characterization of the guinea pig cytomegalovirus UL83 (pp65) protein homolog.
AUTHOR: Schleiss M R; McGregor A; Jensen N J; Erdem G; Aktan L
CORPORATE SOURCE: Division of Infectious Diseases, Children's Hospital Research Foundation, Cincinnati, Ohio 45229, USA.
CONTRACT NUMBER: AI 01276-01 (NIAID)
HD 28827-01 (NICHD)
SOURCE: VIRUS GENES, (1999) 19 (3) 205-21.
Journal code: 8803967. ISSN: 0920-8569.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF131200
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000104

AB The tegument phosphoproteins of human cytomegalovirus (HCMV) elicit

cytotoxic T-lymphocyte (**CTL**) responses and are hence candidates for subunit vaccine development. Little is known, however, about the tegument proteins of nonhuman cytomegaloviruses, such as guinea pig CMV (GPCMV). DNA sequence analysis of the Eco R I "C" fragment of the GPCMV genome **identified** an open reading frame (ORF) which is colinear with that of the HCMV tegument phosphoprotein, UL83 (pp65). This ORF was found to have identity to HCMV UL83 and was predicted to encode a 565-amino-acid (aa) protein with a molecular mass of 62.3 kDa. Transcriptional analyses revealed that a GPCMV UL83 probe **hybridized** with both 2.2 kb and 4.2 kb mRNA species at 48 h post-**infection** (p.i.); synthesis of these messages was blocked by phosphonoacetic acid (PAA), defining these as "late" **gene** transcripts. In vitro translation of the UL83 ORF in reticulocyte lysate resulted in synthesis of a 65 kDa protein. Immunofluorescence experiments revealed that the putative GPCMV UL83 homolog exhibited a predominantly nuclear localization pattern. Polyclonal antisera were raised against a UL83/glutathione-S-transferase (GST) fusion protein. This antibody **identified** a 70-kDa virion-associated protein, the putative GPCMV UL83 homolog, in immunoblot and radioimmunoprecipitation experiments. Labeling experiments with 32P-orthophosphate indicated that the GPCMV UL83 protein is phosphorylated. Western blot analysis of glycerol tartrate gradient-purified virions and dense bodies confirmed that the putative GPCMV UL83 homolog was a constituent of both fractions.

L10 ANSWER 9 OF 53 MEDLINE
ACCESSION NUMBER: 1999242278 MEDLINE
DOCUMENT NUMBER: 99242278 PubMed ID: 10227719
TITLE: CD95 (Fas) ligand expression of Epstein-Barr virus (EBV)-infected lymphocytes: a possible mechanism of immune evasion in chronic active EBV **infection**.
AUTHOR: Ohshima K; Suzumiya J; Sugihara M; Nagafuchi S; Ohga S; Kikuchi M
CORPORATE SOURCE: Department of Pathology, School of Medicine, Fukuoka University, Japan.
SOURCE: PATHOLOGY INTERNATIONAL, (1999 Jan) 49 (1) 9-13. Journal code: 9431380. ISSN: 1320-5463.
PUB. COUNTRY: Australia
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990628
Last Updated on STN: 19990628
Entered Medline: 19990611

AB The Epstein-Barr virus (EBV) induces **infectious** mononucleosis (IM) and can be associated with chronic active EBV **infection** (CAEBV). **Cytotoxic T lymphocytes** (**CTL**) play an important role in excluding EBV-infected cells. Two cytotoxic mechanisms of **CTL** have been demonstrated: one perforin/granzyme-based and the other Fas (CD95)/Fas ligand (FasL)-based. To clarify these two pathways in CAEBV, we analyzed six patients with CAEBV and four patients with IM using immunohistochemical staining of the lymph nodes. In both CAEBV and IM, CD8+ T-cells increased in number, but CD56+ natural killer cells were rare. In four of six cases with

CAEBV, approximately half the lymphocytes were positive for T cell-restricted intracellular **antigens** (TIA-1), which were recognized by the cytolytic granules of **CTL**. In IM, the number of TIA-1 positive cells was smaller than that in CAEBV. Fas-positive lymphocytes were frequently encountered in both CAEBV and IM. However, FasL-positive lymphocytes increased in three of six patients with CAEBV, but not in patients with IM. Except for one case with CAEBV, the number of perforin- and/or granzyme-positive cells was small in number in both CAEBV and IM cases. In double-staining FasL and EBV in situ **hybridization**, FasL-positive EBV-infected lymphocytes were **detected** in CAEBV but not in IM. In CAEBV, the Fas/FasL pathway and not perforin pathways appears to play an important role in the pathogenesis. The data suggest that EBV-infected lymphocytes may evade immune attack through the expression of FasL.

L10 ANSWER 10 OF 53 MEDLINE
ACCESSION NUMBER: 1998223036 MEDLINE
DOCUMENT NUMBER: 98223036 PubMed ID: 9563572
TITLE: Preliminary evidence for an association of Epstein-Barr virus with pre-ulcerative oral lesions in patients with recurrent aphthous ulcers or Behcet's disease.
AUTHOR: Sun A; Chang J G; Chu C T; Liu B Y; Yuan J H; Chiang C P
CORPORATE SOURCE: School of Dentistry, National Taiwan University, Taipei, ROC.
SOURCE: JOURNAL OF ORAL PATHOLOGY AND MEDICINE, (1998 Apr) 27 (4) 168-75.
Journal code: 8911934. ISSN: 0904-2512.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980618
Last Updated on STN: 19980618
Entered Medline: 19980609

AB In this study we used the polymerase chain reaction (PCR), slot blot and Southern blot **hybridization**, direct sequencing and in situ **hybridization** (ISH) to show the possible presence of EBV-DNA in pre-ulcerative oral aphthous lesions of patients with recurrent aphthous ulcers (RAU) or Behcet's disease (BD). For this purpose, formalin-fixed biopsy specimens were obtained from 13 pre-ulcerative oral aphthous lesions of nine RAU and four BD patients. Five specimens of normal oral mucosa (NOM) from five normal control subjects and 10 specimens of oral erosive or ulcerative lesions from 10 patients with erosive lichen planus (ELP) were also included. EBV-DNA was **detected** by PCR in 5 of the 13 (38.5%) pre-ulcerative oral aphthous lesions, two from RAU patients and three from BD patients. However, no EBV-DNA was demonstrated in five NOM specimens from normal control subjects and in 10 specimens of oral lesions from ELP patients. EBV-DNA was also demonstrated in patients' peripheral blood lymphocytes and/or plasma, suggesting that the lymphocytes may be the reservoir of latent EBV **infection** and there is EBV shedding in the plasma. EBV-DNA was **detected** by ISH in only one PCR-positive case; the reaction product was found to deposit on the

nuclei of some of the epithelial cells and lymphocytes. By immunohistochemistry, expression of Epstein-Barr nuclear **antigen** and EBV/C3d receptors was also noted in some of the epithelial cells and lymphocytes in this ISH-positive case. Therefore, we suggest that the epithelial cells of pre-ulcerative oral aphthous lesions may be infected by EBV through EBV-infected lymphocytes; also, the **cytotoxic T lymphocyte**-induced lysis of the EBV-infected epithelial cells, but not the virus-induced cytolysis, may be the main mechanism causing oral ulcer formation. Our data provide preliminary evidence for an association of EBV with pre-ulcerative oral aphthous lesions in RAU and BD patients.

L10 ANSWER 11 OF 53 MEDLINE
ACCESSION NUMBER: 97413372 MEDLINE
DOCUMENT NUMBER: 97413372 PubMed ID: 9269787
TITLE: Immunohistochemical **detection** of the Epstein-Barr virus-encoded latent membrane protein 2A in Hodgkin's disease and **infectious** mononucleosis.
AUTHOR: Niedobitek G; Kremmer E; Herbst H; Whitehead L; Dawson C W; Niedobitek E; von Ostau C; Rooney N; Grasser F A; Young L S
CORPORATE SOURCE: Institute for Cancer Studies and the Department of Pathology, University of Birmingham, UK.
SOURCE: BLOOD, (1997 Aug 15) 90 (4) 1664-72.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19971008
Last Updated on STN: 19980206
Entered Medline: 19970924

AB We describe two new monoclonal antibodies specific for the Epstein-Barr virus (EBV)-encoded latent membrane protein 2A (LMP2A) that are suitable for the immunohistochemical analysis of routinely processed paraffin sections. These antibodies were applied to the immunohistochemical **detection** of LMP2A in Hodgkin's disease (HD). LMP2A-specific membrane staining was seen in the Hodgkin and Reed-Sternberg (HRS) cells of 22 of 42 (52%) EBV-positive HD cases, but not in 39 EBV-negative HD cases. In lymphoid tissues from patients with acute **infectious** mononucleosis (IM), interfollicular immunoblasts were shown to express LMP2A. This is the first demonstration of LMP2A protein expression at the single-cell level in EBV-associated lymphoproliferations in vivo. The **detection** of LMP2A protein expression in HD and IM is of importance in view of the proposed role of this protein for maintaining latent EBV **infection** and its possible contribution for EBV-associated transformation. Because LMP2A provides target epitopes for EBV-specific **cytotoxic T cells**, the expression of this protein in HRS cells has implications for the immunotherapeutic approaches to the **treatment** of HD.

L10 ANSWER 12 OF 53 MEDLINE
ACCESSION NUMBER: 94377506 MEDLINE

DOCUMENT NUMBER: 94377506 PubMed ID: 8090780
TITLE: Gastric carcinoma: monoclonal epithelial malignant cells expressing Epstein-Barr virus latent **infection** protein.
AUTHOR: Imai S; Koizumi S; Sugiura M; Tokunaga M; Uemura Y; Yamamoto N; Tanaka S; Sato E; Osato T
CORPORATE SOURCE: Department of Virology, Hokkaido University School of Medicine, Sapporo, Japan.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Sep 13) 91 (19) 9131-5.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941031
Last Updated on STN: 19941031
Entered Medline: 19941014

AB In 1000 primary gastric carcinomas, 70 (7.0%) contained Epstein-Barr virus (EBV) genomic sequences **detected** by PCR and Southern blots. The positive tumors comprised 8 of 9 (89%) undifferentiated lymphoepithelioma-like carcinomas, 27 of 476 (5.7%) poorly differentiated adenocarcinomas, and 35 of 515 (6.8%) moderately to well-differentiated adenocarcinomas. In situ EBV-encoded small RNA 1 **hybridization** and hematoxylin/eosin staining in adjacent sections showed that the EBV was present in every carcinoma cell but was not significantly present in lymphoid stroma and in normal mucosa. Two-color immunofluorescence and hematoxylin/eosin staining in parallel sections revealed that every keratin-positive epithelial malignant cell expressed EBV-**determined** nuclear **antigen** 1 (EBNA1) but did not significantly express CD45+ infiltrating leukocytes. A single fused terminal fragment was **detected** in each of the EBNA1-expressing tumors, thereby suggesting that the EBV-carrying gastric carcinomas represent clonal proliferation of cells infected with EBV. The carcinoma cells had exclusively EBNA1 but not EBNA2, -3A, -3B, and -3C; leader protein; and latent membrane protein 1 because of methylation. The patients with EBV-carrying gastric carcinoma had elevated serum EBV-specific antibodies. The EBV-specific cellular immunity was not significantly reduced; however, the **cytotoxic T-cell** target **antigens** were not expressed. These findings strongly suggest a causal relation between a significant proportion of gastric carcinoma and EBV, and the virus-carrying carcinoma cells may evade immune surveillance.

L10 ANSWER 13 OF 53 MEDLINE
ACCESSION NUMBER: 94268691 MEDLINE
DOCUMENT NUMBER: 94268691 PubMed ID: 7516054
TITLE: Expression of **HIV**-1 and interleukin-6 in lumbosacral dorsal root ganglia of patients with **AIDS**.
COMMENT: Erratum in: Neurology 1994 Aug;44(8):1504-5
AUTHOR: Yoshioka M; Shapshak P; Srivastava A K; Stewart R V; Nelson S J; Bradley W G; Berger J R; Rhodes R H; Sun N C; Nakamura S
CORPORATE SOURCE: Department of Psychiatry, University of Miami School

of Medicine, FL.
CONTRACT NUMBER: NIDA DA 04787 (NIDA)
NIDA DA 07909 (NIDA)
NINDS NS 26584 (NINDS)
+
SOURCE: NEUROLOGY, (1994 Jun) 44 (6) 1120-30.
Journal code: 0401060. ISSN: 0028-3878.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940721
Last Updated on STN: 19970203
Entered Medline: 19940713

AB We examined the immunopathology and the expression of **human** immunodeficiency **virus** type 1 (**HIV**-1) in lumbosacral dorsal root ganglia (DRGs) from 16 patients with **acquired** immunodeficiency **syndrome** (**AIDS**) and 10 **HIV**-1-seronegative controls. Using in situ **hybridization**, we **detected HIV**-1 RNA in a few perivascular cells in DRGs from five of 16 **AIDS** patients (31%). In addition, using polymerase chain reaction, we **detected HIV**-1 DNA more frequently in DRGs from four of five **AIDS** patients (80%) examined. We **detected** interleukin-6 (IL-6) immunoreactivity in endothelial cells in DRGs from seven of 16 **AIDS** patients (44%) but from none of 10 **HIV**-1-seronegative controls (0%). We found more nodules of Nageotte, CD8+ T lymphocytes, and intercellular adhesion molecule-1 (ICAM-1)-positive endothelial cells and mononuclear cells in DRGs from **AIDS** patients than in DRGs from controls. Increased numbers of nodules of Nageotte in DRGs of **AIDS** patients were associated with **detection** of **HIV**-1 RNA by in situ **hybridization** and **detection** of IL-6 by immunohistochemistry. We conclude that low levels of replication of **HIV**-1, through **cytotoxic T lymphocytes** or expression of cytokines, may play a role in the subclinical degeneration of sensory neurons frequently observed in DRGs of **AIDS** patients.

L10 ANSWER 14 OF 53 MEDLINE
ACCESSION NUMBER: 94187077 MEDLINE
DOCUMENT NUMBER: 94187077 PubMed ID: 8139022
TITLE: Immunopathogenic events in acute **infection** of rhesus monkeys with simian immunodeficiency virus of macaques.
AUTHOR: Reimann K A; Tenner-Racz K; Racz P; Montefiori D C; Yasutomi Y; Lin W; Ransil B J; Letvin N L
CORPORATE SOURCE: New England Regional Primate Research Center, Harvard Medical School, Southborough, Massachusetts 01772.
CONTRACT NUMBER: AI-20729 (NIAID)
CA-50139 (NCI)
RR-000168 (NCRR)
+
SOURCE: JOURNAL OF VIROLOGY, (1994 Apr) 68 (4) 2362-70.
Journal code: 0113724. ISSN: 0022-538X.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940509
Last Updated on STN: 19970203
Entered Medline: 19940425

AB **Infection** of the rhesus monkey with simian immunodeficiency virus of macaques (SIVmax) was employed to explore the early immune events associated with the initial containment of an acute **AIDS** virus **infection**. In nine rhesus monkeys infected intravenously with uncloned SIVmac strain 251, high-level p27 plasma **antigenemia** was usually **detected** transiently from approximately day 7 through day 21 following virus inoculation. SIVmac replication in lymph nodes measured by in situ RNA **hybridization** closely paralleled the time course and magnitude of viremia. The containment of SIVmac spread by 3 to 4 weeks following **infection** suggests an efficient, early immune control of this virus **infection**. Anti-SIVmac antibodies were first **detected** in the blood at approximately day 14. At the time **antigenemia** was decreased or cleared, SIVmac neutralizing antibodies were present. A rise in circulating and lymph node CD8+ T cells also occurred coincident with the clearance of **antigenemia** and persisted thereafter. These CD8+ lymphocytes in lymph nodes had increased expression of both major histocompatibility complex class II and the adhesion molecule LFA-1; they also demonstrated decreased expression of the naive T-cell-associated CD45RA molecule. SIVmac-specific **cytotoxic T-lymphocyte** precursors were **detected** in both blood and lymph node by 7 days post-virus inoculation. These studies indicate that both virus-specific humoral and cellular immune mechanisms in blood and lymph node are associated with the clearance of viremia that occurs within the first month of **infection** of rhesus monkeys with SIVmac.

L10 ANSWER 15 OF 53 MEDLINE
ACCESSION NUMBER: 93275906 MEDLINE
DOCUMENT NUMBER: 93275906 PubMed ID: 8502679
TITLE: Immunisation of woodchucks with hepatitis delta **antigen** expressed by recombinant vaccinia and baculoviruses, controls HDV superinfection.
AUTHOR: Karayiannis P; Saldanha J; Monjardino J; Jackson A; Luther S; Thomas H C
CORPORATE SOURCE: Department of Medicine, St. Mary's Hospital Medical School, London, U.K.
SOURCE: PROGRESS IN CLINICAL AND BIOLOGICAL RESEARCH, (1993) 382 193-9.
Journal code: 7605701. ISSN: 0361-7742.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199307
ENTRY DATE: Entered STN: 19930716
Last Updated on STN: 19980206
Entered Medline: 19930701

AB We report the investigation of the role of humoral and cell mediated

immune responses on hepatitis delta virus (HDV) superinfection of woodchucks chronically infected with woodchuck hepatitis virus (WHV). The animals were immunised with baculovirus or vaccinia virus recombinant hepatitis delta **antigen** (HDAg) but none showed **detectable** anti-HD titres prior to challenge with HDV. Following **infection**, both immunised and control animals developed HD-**antigenaemia** first **detected** after 2-3 weeks and lasting for up to 8 weeks. In spite of the presence of HDAg, in immunised animals HDV-RNA could only be **detected** by nested PCR in contrast with the controls, which were positive by dot blot **hybridisation**. No serum HDAg or HDV-RNA was **detected** after the acute episode over the six month follow-up period but intrahepatic HDAg was reported in post-mortem biopsies carried out at six months. Our results demonstrate that immunisation of woodchucks with HDAg expressed by vaccinia or baculovirus does not elicit a humoral immune response. The finding of a marked **antigenaemia** in the absence of serum HDV-RNA indicates a significant reduction in the number of circulating **infectious** virions possibly due to a **cytotoxic T-cell** response.

L10 ANSWER 16 OF 53 MEDLINE
ACCESSION NUMBER: 93147723 MEDLINE
DOCUMENT NUMBER: 93147723 PubMed ID: 8381153
TITLE: Epstein-Barr virus and Hodgkin's disease: transcriptional analysis of virus latency in the malignant cells.
AUTHOR: Deacon E M; Pallesen G; Niedobitek G; Crocker J; Brooks L; Rickinson A B; Young L S
CORPORATE SOURCE: Department of Cancer Studies, University of Birmingham Medical School, United Kingdom.
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1993 Feb 1) 177 (2) 339-49.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 19930312
Last Updated on STN: 19980206
Entered Medline: 19930301

AB Epstein-Barr virus (EBV) is associated with a number of different human tumors and appears to play different pathogenetic roles in each case. Thus, immunoblastic B cell lymphomas of the immunosuppressed display the full pattern of EBV latent **gene** expression (expressing Epstein-Barr nuclear **antigen** [EBNA]1, 2, 3A, 3B, 3C, and -LP, and latent membrane protein [LMP]1, 2A, and 2B), just as do B lymphoblastoid cell lines transformed by the virus in vitro. In contrast, those EBV-associated tumors with a more complex, multistep pathogenesis show more restricted patterns of viral **gene** expression, limited in Burkitt's lymphoma to EBNA1 only and in nasopharyngeal carcinoma (NPC) to EBNA1 and LMP1, 2A, and 2B. Recent evidence has implicated EBV in the pathogenesis of another lymphoid tumor, Hodgkin's disease (HD), where the malignant Hodgkin's and Reed-Sternberg (HRS) cells are EBV genome positive in up to 50% of cases. Here we extend preliminary results on viral **gene** expression in HRS cells by adopting

polymerase chain reaction-based and in situ **hybridization** assays capable of **detecting** specific EBV latent transcripts diagnostic of the different possible forms of EBV latency. We show that the transcriptional program of the virus in HRS cells is similar to that seen in NPC in several respects: (a) selective expression of EBNA1 mRNA from the BamHI F promoter; (b) downregulation of the BamHI C and W promoters and their associated EBNA mRNAs; (c) expression of LMP1 and, in most cases, LMP2A and 2B transcripts; and (d) expression of the "rightward-running" BamHI A transcripts once thought to be unique to NPC. This form of latency, consistently **detected** in EBV-positive HD irrespective of histological subtype, implies an active role for the virus in the pathogenesis of HD and also suggests that the tumor may remain sensitive to at least certain facets of the EBV-induced **cytotoxic T cell** response.

L10 ANSWER 17 OF 53 MEDLINE
ACCESSION NUMBER: 92029722 MEDLINE
DOCUMENT NUMBER: 92029722 PubMed ID: 1930770
TITLE: Activation of cytotoxic cells in hyperplastic lymph nodes from **HIV**-infected patients.
AUTHOR: Devergne O; Peuchmaur M; Crevon M C; Trapani J A; Maillot M C; Galanaud P; Emilie D
CORPORATE SOURCE: INSERM U131, Clamart, France.
SOURCE: AIDS, (1991 Sep) 5 (9) 1071-9.
Journal code: 8710219. ISSN: 0269-9370.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19970203
Entered Medline: 19911212

AB Serine esterase B (SE B) is a protein contained in cytoplasmic granules of **cytotoxic T lymphocytes** and natural killer cells; SE B **gene** is transcribed upon activation of these cytotoxic cells. In order to show the in vivo interactions between **HIV**-infected cells and anti-**HIV** cytotoxic cells we analysed, by in situ **hybridization**, the expression of the SE B **gene** in eight hyperplastic lymph nodes from **HIV**-1-infected patients presenting with persistent generalized lymphadenopathy. We **detected** numerous cells expressing the SE B **gene**. The mean number of positive cells was 3.2 times higher in **HIV** lymph nodes than in six non-**HIV** hyperplastic lymph nodes studied in parallel (P less than 0.05). In control lymph nodes, the SE B **gene** was expressed only in interfollicular areas; virtually no cells expressed the SE B **gene** within follicles. In contrast, in **HIV** lymph nodes cells expressing the SE B **gene** were distributed either in interfollicular areas or within follicles. Expression of the SE B **gene** inside follicles was thus a specific feature of **HIV** lymph nodes (P less than 0.001) and was associated with the presence of **HIV antigens** and RNA at the same site. These results suggest that cytotoxic cells are activated in follicles of **HIV** lymph nodes and may be involved in the lysis of **HIV**-infected cells. Such a phenomenon may explain

the development of follicle lysis, a specific feature of **HIV** lymph nodes. It may also inhibit the spreading of **HIV infection.**

L10 ANSWER 18 OF 53 MEDLINE
ACCESSION NUMBER: 92012857 MEDLINE
DOCUMENT NUMBER: 92012857 PubMed ID: 1918877
TITLE: Serum HBV DNA **detected** by PCR in dot blot negative HBV chronic carriers with active liver disease.
AUTHOR: Monjardino J; Velosa J; Thomas H C; de Moura M C
CORPORATE SOURCE: Academic Department of Medicine, St. Mary's Hospital Medical School, London, United Kingdom.
SOURCE: JOURNAL OF HEPATOLOGY, (1991 Jul) 13 (1) 44-8. Journal code: 8503886. ISSN: 0168-8278.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199111
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19920124
Entered Medline: 19911114

AB A group of forty-nine HBV chronic carriers with histologically confirmed active liver disease and undetected serum HBV DNA by dot-blot **hybridisation** were re-investigated using the polymerase chain reaction (PCR) for amplification of serum DNA. The group comprised 16 persistently serum HBeAg-negative and thirty-three anti-HBe-positive patients. The use of PCR followed by Southern blot analysis has increased the sensitivity of HBV DNA **detection** to about 10-50 virions per ml of serum. Our results showed 14/16 (87.5%) of the HBeAg-positive group and 27/33 (81.8%) of the anti-HBe group to be positive for HBV DNA using PCR. Of the nine cases where HBV DNA was undetected four were positive for markers of hepatitis delta virus (HDV) **infection.** Demonstration of low level HBV replication associated with active liver disease in chronic HBV carriers where it was previously undetected meets a basic requirement for the proposed role of **cytotoxic T lymphocyte**-mediated immunopathogenesis in chronic hepatitis B and suggests a combined antiviral and immunotherapeutic approach to achieve eradication of the **infection.**

L10 ANSWER 19 OF 53 MEDLINE
ACCESSION NUMBER: 91170737 MEDLINE
DOCUMENT NUMBER: 91170737 PubMed ID: 1672337
TITLE: The role of CD4+ cells in sustaining lymphocyte proliferation during lymphocytic choriomeningitis virus **infection.**
AUTHOR: Kasaian M T; Leite-Morris K A; Biron C A
CORPORATE SOURCE: Division of Biology and Medicine, Brown University, Providence, RI 02912.
CONTRACT NUMBER: CA-41268 (NCI)
SOURCE: JOURNAL OF IMMUNOLOGY, (1991 Mar 15) 146 (6) 1955-63. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199104
ENTRY DATE: Entered STN: 19910512
Last Updated on STN: 19950206
Entered Medline: 19910422

AB The murine immune response to lymphocytic choriomeningitis virus (LCMV) **infection** involves the activation of CD8+, class I MHC-restricted and virus-specific **CTL**. At times coinciding with **CTL** activation, high levels of IL-2 **gene** expression and production occur, the IL-2R is expressed, and T cell blastogenesis and proliferation are induced. We have previously found that, although both CD4+ and CD8+ T cell subsets transcribe IL-2, the CD4+ subset appears to be the major producer of IL-2 whereas the CD8+ subset appears to be the major proliferating population when the subsets are separated after activation in vivo. The studies presented here were undertaken to examine the contribution made by the CD4+ subset to lymphocyte proliferation in vivo. Responses to LCMV **infection** were examined in intact mice and in mice depleted of CD4+ or CD8+ subsets by antibody **treatments** in vivo. Protocols were such that in vivo **treatments** with anti-CD4 or anti-CD8 depleted the respective subset by greater than 90%. In situ **hybridizations** demonstrated that the IL-2 **gene** was expressed in non-B lymphocytes isolated from either CD4+ cell-depleted or CD8+ cell-depleted mice on day 7 post-**infection** with LCMV. When placed in culture, however, cells from CD8+ cell-depleted mice produced significantly higher levels of **detectable** IL-2 than did cells isolated from CD4+ cell-depleted mice on day 7 post-**infection**. IL-2 was apparently produced in vivo in mice depleted of either CD4+ or CD8+ cells, as expression of the **gene** for the p55 chain of the IL-2R, IL-2 responsiveness, and lymphocyte proliferation were observed with cells isolated from both sets of mice. Lymphocyte proliferation was shown to be sustained in mice depleted of CD4+ cells in vivo by three criteria: 1) non-B lymphocytes isolated from infected mice depleted of CD4+ cells underwent more DNA synthesis than did those isolated from uninfected mice or from infected mice depleted of CD8+ cells; 2) leukocyte yields were expanded during **infection** of CD4+ cell-depleted mice; and 3) CD8+ cell numbers were increased during **infection** of CD4+ cell-depleted mice. The majority of non-B lymphocytes having the characteristics of blast lymphocytes was recovered in the CD8+ populations isolated from infected CD4+ cell-depleted mice. These findings suggest that the requirement for the CD4+ subset to sustain CD8+ lymphocyte proliferation in vivo is limited, and that CD4+ and CD8+ cell types can function independently in many aspects of their responses to viral **infections**.

L10 ANSWER 20 OF 53 MEDLINE
ACCESSION NUMBER: 88140307 MEDLINE
DOCUMENT NUMBER: 88140307 PubMed ID: 2963865
TITLE: Virus-lymphocyte interactions. II. Expression of viral sequences during the course of persistent lymphocytic choriomeningitis virus **infection** and their localization to the L3T4 lymphocyte subset.
AUTHOR: Tishon A; Southern P J; Oldstone M B
CORPORATE SOURCE: Department of Immunology, Research Institute of Scripps Clinic, La Jolla, CA 92037.

CONTRACT NUMBER: AG-04342 (NIA)
AI-09484 (NIAID)
NS-12428 (NINDS)
SOURCE: JOURNAL OF IMMUNOLOGY, (1988 Feb 15) 140 (4) 1280-4.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198804
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880405

AB Viruses that cause in vivo persistent **infections** need to selectively compromise the host's immunologic surveillance machinery in order to survive. To understand the molecular basis of how this is accomplished we have analyzed persistent virus **infection** by lymphocytic choriomeningitis in its normal host, the mouse. Earlier we noted by **infectious** center analysis that five in 10(4) lymphocytes carried by persistently infected mice contained **infectious** materials throughout the course of **infection**. A previous publication extended these results, in BALB mice by showing that the L3T4+ lymphocyte subset in lymph nodes and spleens was predominantly involved. Using cDNA labeled probes to the viral genome and in situ **hybridization** we report that 1 to 2% of circulating lymphocytes from several mouse strains contain viral RNA sequences for the three viral structural **genes**. By FACS analysis, the Thy-1.2+, L3T4+ subset primarily harbors virus while viral sequences are usually not **detected** in the Lyt-2+ subset as early as 6 days after initiating **infection** in newborns and throughout the course of the persistence. These findings suggest that incomplete, presumably defective, virus is generated in a subset of Th lymphocytes during persistent **infection** and that during this time **infection** of **cytotoxic T cell** subsets is minimal.

L10 ANSWER 21 OF 53 MEDLINE
ACCESSION NUMBER: 86149322 MEDLINE
DOCUMENT NUMBER: 86149322 PubMed ID: 2869486
TITLE: Hybrid hybridoma producing a bispecific monoclonal antibody that can focus effector T-cell activity.
AUTHOR: Staerz U D; Bevan M J
CONTRACT NUMBER: AI19335 (NIAID)
CA25803 (NCI)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1986 Mar) 83 (5) 1453-7.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198604
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860410

AB Previous studies have shown that heteroconjugates of monoclonal

(2)

STIC STN Search Report

09/966746

D. M. (1)
CORPORATE SOURCE: (1) Pathology, Weill Medical College of Cornell University, New York, NY USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 505a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology . ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB PT-LPDs are a complication of solid organ (SOT) and bone marrow (BMT) transplantation. PT-LPDs in both are Epstein-Barr virus (EBV) driven, but may be different pathogenically since SOT PT-LPDs are usually of recipient while BMT PT-LPDs are of donor origin. We have shown that **genetic** alterations, rather than mechanisms associated with EBV **infection**, dictate the biological behavior of SOT PT-LPDs. However the pathogenetic mechanisms associated with PT-LPDs in BMT have not been fully elucidated. We studied 94 frozen and 158 fixed tissues from 46 BMT recipients. Frozen tissue was examined for IgH **gene** clonality and the presence/type of EBV by PCR. Paraffin tissues were studied for EBV **gene** expression by in situ **hybridization** (EBER) and immunostaining (LMP-1, EBNA-2). Lesions were classified based on the criteria of Knowles and Frizzera. Clinical information was available in 43 pts. Morphologically, 86 specimens from 26 pts (12 males, 14 females) contained PT-LPD. Lesions developed 1-17.5 mo. post BMT (median 4.1 mo); 14 pts had received anti-CD3 **therapy** or T cell depleted BM. 11 PT-LPDs were classified as plasmacytic hyperplasia (PH), 50 as polymorphic B cell hyperplasia (PBCH), 21 as polymorphic B cell lymphoma (PBCL), 4 had features of PBCH and PBCL; no non-Hodgkin's lymphoma or myeloma cases were **identified**. In 7 pts separate PT-LPDs exhibited different morphology. Analysis of IgH **gene** rearrangements by PCR showed variable clonality: PBCH/ PBCL: 77% mono- or oligoclonal (MC/OC) and 23% polyclonal (PC); PH: 38% MC/OC and 62% PC. 21/25 (84%) pts had EBV positive lesions by PCR (17; type A=15; type B=2) or ISH (4). All cases positive for EBV by PCR/ISH expressed one or both of the EBV immunogenic / transforming **antigens** (EBNA2, LMP1). The majority of PBCH/PBCLs exhibited the latency type III (92%) while 80% of PHs exhibited the latency type II pattern. PT-LPD was the cause of death in 67% of pts; all were EBV positive. EBV negative pts died of other causes. In summary, BMT PT-LPDs: (1) present as widespread, rapidly fulminant disease; (2) often exhibit the PBCH pattern; and (3) if EBV positive, express the immunogenic **antigens** LMP1 and EBNA2. Thus, EBV may play a more important role in the biologic behavior of BMT PT-LPDs than in SOT PT-LPDs partially explaining the generally good clinical response of BMT PT-LPDs to EBV-specific donor **cytotoxic T lymphocyte** infusions.

L10 ANSWER 24 OF 53 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:293781 BIOSIS
DOCUMENT NUMBER: PREV200100293781
TITLE: Characterization of autoreactive T-cells in aplastic anemia.
AUTHOR(S): Zeng, Weihua (1); Maciejewski, Jaroslaw P. (1);

Young, Neal S. (1)
CORPORATE SOURCE: (1) Hematology Branch, National Heart, Lung, and Blood Institute, Bethesda, MD USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 5a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology . ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Despite progress in understanding the pathophysiology of aplastic anemia (AA), the **antigens** that drive immune-mediated stem cell destruction are not **identified**. Response to immunosuppression remains the strongest clinical evidence of an immune pathophysiology, bolstered by laboratory demonstration of a proximal Th1 process involving **cytotoxic T cell** activation, gamma-interferon expression, and Fas-mediated apoptosis of CD34 cells. Early events are not well characterized. Inciting **antigens** could arise from molecular mimicry with **infectious** agents or from proteins modified by drug/chemical interaction; over or aberrant expression of normal self **antigens** might also be immunogenic. We examined the T-cell receptor (TCR) repertoire of lymphocyte clones derived from a patient with the AA/PNH syndrome; his HLA **antigens** were A32 A33, B35 B51; DR11, DR15. T cells showed an activated phenotype and displayed marked Vbeta skewing, especially of Vbeta13 and Vbeta5. T-cell lines were established from sorted CD4 and CD8 cells, in which CD69 expression indicated in vivo activation. A total of 105 CD4 and 30 CD8 cell clones were immortalized using herpesvirus saimiri. TCRs of these clones was analyzed using polymerase chain reaction with Vbeta-specific primers. Most (24/30) activated CD4 clones displayed Vbeta5 TCR and the majority (8/12) of CD8 clones expressed Vbeta13. Sequence analysis of the TCR CDR3 region revealed identity for all CD4 Vbeta5 and CD8 Vbeta13 clones, respectively, suggesting that these TCR were over-utilized among activated T-cells. In vitro, T-cell clones carrying the specific TCR were cytotoxic for CD34 cells and inhibited hematopoietic colony formation in vitro for patient target cells, but not for HLA-matched normal marrow targets. A representative CD4 clone showed a Th1 secretion pattern, while a CD8 clone was of the terminal effector phenotype (CD45RO, CD28-, CD57). By specific PCR, we found that the same Vbeta5 spectratype was also present in 11/30 AA patients bearing the DR15 haplotype and 5/7 matched for HLA-B Vbeta13 spectratype. We were unable to **detect** these specific TCR sequences among normal, HLA-matched individuals. As quantitated by Southern **hybridization** of TCR Vbeta PCR products using specific CDR3 probes, the numbers of T-cell displaying these spectratype decreased in 3/4 patients responding to immunosuppressive **therapy**. These striking TCR similarities suggest first, that there is limited heterogeneity in the T cell response in individual patients and, second, that AA patients may recognize similar **antigens**. Furthermore, these T cell clones should be useful to **identify** target peptides in expression libraries that activate autoreactive T cells.

L10 ANSWER 25 OF 53 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1993:186996 BIOSIS
DOCUMENT NUMBER: PREV199395097446
TITLE: Lymphokine expression profile of resting and stimulated CD4-positive **CTL** clones specific for the glycoprotein of vesicular stomatitis virus.
AUTHOR(S): Cao, Ben-Ning; Huneycutt, Brandon S.; Gapud, Carolina P.; Arceci, Robert J.; Reiss, Carol S. (1)
CORPORATE SOURCE: (1) Biol. Deo., New York Univ., Main Build. Room 1009, 100 Washington Sq. East, New York, N.Y. 10003
SOURCE: Cellular Immunology, (1993) Vol. 146, No. 1, pp. 147-156.
ISSN: 0008-8749.
DOCUMENT TYPE: Article
LANGUAGE: English
AB A panel of long-term murine T lymphocyte clones specific for the glycoprotein of vesicular stomatitis virus (VSV) in association with either H-2I-A-d or I-E-d was tested for the production of cytokines in both resting and poststimulation states using both in situ **hybridization** and bioassay. All but one of the clones showed **antigen**-specific cytolytic activity in a 4-hr 51Cr release assay. Unexpectedly, the clones did not appear to be typical Th1 cells. Five of these T cell clones produced both IL-2 and IFN-gamma but not IL-4 after stimulation with either phorbol 12-myristate 13-acetate (PMA) or concanavalin A (Con A). Some clones constitutively expressed mRNA for IL-2 and INF-gamma. The proliferation of these clones was factor independent, suggesting an autocrine growth mechanism. Three clones produced variable levels of IL-4 mRNA and some, to significant quantities, of IL-2 mRNA. One cytolytic clone produced neither IL-2 nor IL-4 mRNA to **detectable** levels, although mRNA for IFN-gamma was observed. A noncytolytic, Ag-specific clone produced IL 6, tumor necrosis factor (TNF), and lymphotoxin (LT), but no IL-2, IL-4, or IFN-gamma mRNA. There was a strong quantitative correlation between the expression of IL-2-, INF-gamma-, and LT specific mRNAs by the clones. All the T cell clones tested which secreted INF-gamma and LT expressed no measurable IL-4 mRNA. We examined expression of several other **genes** in the panel of clones. These included TNF, met-enkephalin (met-enk), IL-1, and IL-6, IL-1 m-RNA synthesis was not observed in any of the T cell clones. Almost all clones produced TNF mRNA. Parallel bioassays showed that secreted IL-2/IL-4 activity levels and mRNA levels correlated well for all clones. Thus, we observed a great degree of heterogeneity among CD4+ cytolytic T lymphocyte clones.

L10 ANSWER 26 OF 53 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1987:380372 BIOSIS
DOCUMENT NUMBER: BA84:66869
TITLE: THE E3-19K PROTEIN OF ADENOVIRUS TYPE 2 BINDS TO THE DOMAINS OF HISTOCOMPATIBILITY **ANTIGENS** REQUIRED FOR **CTL** RECOGNITION.
AUTHOR(S): BURGERT H-G; KVIST S
CORPORATE SOURCE: HOWARD HUGHES MED. INST., DENVER, COLO. 80206, USA.
SOURCE: EMBO (EUR MOL BIOL ORGAN) J, (1987) 6 (7), 2019-2026.
CODEN: EMJODG. ISSN: 0261-4189.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The E3/19K protein of human adenovirus type 2 binds to HLA class I

antigens and blocks their terminal glycosylation and cell surface expression. The nature of this interaction is non-covalent and involves neither disulfide bridges between the two molecules nor their carbohydrates. The murine H-2 Kd **antigen** associates with the E3/19K protein in a similar fashion to human HLA **antigens** whereas the allelic product H-2 Kk does not. Hybrid **genes** between the Kd and Kk alleles were constructed and their products were expressed in embryonic kidney cells together with the E3/19K protein. This allowed us to **identify** the .alpha.1 and .alpha.2 domains as the essential structures of the histocompatibility **antigens** for binding the viral protein. Interestingly, these domains are also crucial for T cell recognition. The implications for the evolution of adenoviruses and their ability to cause persistent **infections** are discussed.

L10 ANSWER 27 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001345987 EMBASE
TITLE: Editorial comment on **detection** of Epstein-Barr virus DNA in peripheral blood of paediatric patients with Hodgkin's disease by real-time polymerase chain reaction by Wagner and colleagues.
AUTHOR: Magrath I.
CORPORATE SOURCE: I. Magrath, Intl. Network for Can. Treat./Res., Brussels, Belgium. imagrath@inctr.be
SOURCE: European Journal of Cancer, (2001) 37/15 (1812-1815). Refs: 30
ISSN: 0959-8049 CODEN: EJCAEL
PUBLISHER IDENT.: S 0959-8049(01)00221-0
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 004 Microbiology
016 Cancer
037 Drug Literature Index
LANGUAGE: English

L10 ANSWER 28 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000302528 EMBASE
TITLE: Gastrointestinal T cell lymphoma: Predominant cytotoxic phenotypes, including alpha/beta, gamma/delta T cell and natural killer cells.
AUTHOR: Katoh A.; Ohshima K.; Kanda M.; Haraoka S.; Sugihara M.; Suzumiya J.; Kawasaki C.; Shimazaki K.; Ikeda S.; Kikuchi M.
CORPORATE SOURCE: Dr. K. Ohshima, Department of Pathology, School of Medicine, Fukuoka University, Nanakuma 7-45-1, Jonan-ku, Fukuoka 814-01, Japan
SOURCE: Leukemia and Lymphoma, (2000) 39/1-2 (97-111). Refs: 51
ISSN: 1042-8194 CODEN: LELYEA
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Gastrointestinal T cell lymphoma (TCL) is a rare subset of peripheral TCL, presenting with or without cytotoxic phenotype, a history of coeliac disease (CD) and enteropathy. However, CD is rare in Japan. Here, we describe the clinicopathological features of 18 Japanese cases. Lesions were found in the small intestine (n=13), stomach (n=3) and colon (n=2). Seven patients presented with enteropathy but none had a history of CD. Lymphomas appeared as ulceration (n=11), tumour formation (n=6), or polypoid growth (n=1). Histologically (REAL classification), neoplastic lesions were composed of intestinal type T cell lymphoma (ITCL, n=13, including one case with NK type), anaplastic large cell (ALCL, n=2), adult T cell leukaemia/lymphoma (ATLL, n=2), and lymphoblastic type (n=1). Epstein Barr virus **infection** was **detected** by EBER-1 in situ **hybridization** in 6 of 11 cases with ITCL but not in the other types. ALCL expressed CD30. CD56 was expressed in 3 of 11 cases of ITCL but not in other types. Among the 10 examined cases, 8 were .alpha..beta. T cell type [CD2+, CD3+, T cell receptor (TCR).delta.-1-, .beta.F1+], one was .gamma..delta. T cell type [CD2+, CD3+, TCR.delta.-1+, .beta.F1-], and the remaining case expressed natural killer (NK) cell type [CD2+, CD3-, CD56+, TCR.delta.-1-, .beta.F1-]. Among the 8 examined cases, 3 expressed CD103 molecule, which was associated with extrathymic T cells of intraepithelial lymphocytes. All cases except ATLL expressed the cytotoxicity-associated molecule of TIA-1, and 11 of 14 TIA-1 positive cases expressed activated cytotoxic molecules of perforin, granzyme B, and/or Fas ligand. Despite the morphological, **genetic** and phenotypic heterogeneity, prognosis was poor, and 11 of 13 patients with small intestinal lesions died albeit appropriate **treatment**, but 3 of 4 patients with gastric or colonic lesions were still alive. The main cause of death was intestinal perforation. The latter might be due to the site specificity of small intestine and tumour cytotoxicity.

L10 ANSWER 29 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999375428 EMBASE
TITLE: [Epstein-Barr Virus (EBV) **gene** expression during **infectious** mononucleosis]. EPSTEIN-BARR-VIRUS (EBV)-GENEXPRESSION BEI AKUTER INFEKTIOSER MONONUKLEOSE.
AUTHOR: Schuster V.; Pukrop T.; Seldenspinner S.; Schontube M.
CORPORATE SOURCE: Dr. V. Schuster, Universitats-Kinderklinik, Oststrasse 21-25, D-04317 Leipzig, Germany
SOURCE: Monatsschrift fur Kinderheilkunde, (1999) 147/10 (917-920).
Refs: 22
ISSN: 0026-9298 CODEN: MOKIAY
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
025 Hematology
LANGUAGE: German
SUMMARY LANGUAGE: English; German
AB Background: Acute **infectious** mononucleosis (IM) is a selflimiting lymphoproliferative disease of EBV-infected (immortalised) B cells and poly- /oligoclonal **cytotoxic T cells** which are to a high percentage

EBV-specific. In B cells EBV **infection** mainly leads to a latent **infection** with expression of EBV nuclear **antigens** 1-6 (EBNA1-6) and membrane **antigens** 1, 2A and 2B (LMP1, LMP2A and LMP2B). Expression of these EBV latent **antigens** leads to transformation and immortalisation of infected B cells. Here we examined if also lytic EBV **genes** (i.e. BZLF1), which are associated with a productive EBV **infection**, are expressed during IM. Methods: RNA expression of EBV latent **genes** EBNA1, LMP1 and LMP2A and EBV lytic **gene** BZLF1 in peripheral blood mononuclear cells (PBMC) of 12 patients with IM and 1 patient with acute T cell leukemia (HTLVI positive) was studied by nested RT-PCR and subsequent **hybridisation** with an EBV specific oligonucleotide. Results: Expression of latent EBV **genes**, EBNA1, LMP1 and LMP2A, was found in 50%, 83% and 92 %, respectively, of 12 patients with IM. Expression of lytic EBV **gene** BZLF1 was **detected** in 58%. One patient with T cell leukemia exhibited expression of all latent EBV **genes** and of lytic EBV **gene** BZLF1. Conclusion: EBV lytic **gene** BZLF1 is expressed during IM in a high percentage. Certain nucleosidanaloga (i.e. aciclovir and others), which inhibit only lytic but not latent EBV **infection**, may eventually be useful in complicated and chronic EBV **infections**, when EBV lytic **infection** is present.

L10 ANSWER 30 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998111358 EMBASE
TITLE: Virological basis of Epstein-Barr virus-positive gastric carcinoma.
AUTHOR: Imai S.
CORPORATE SOURCE: S. Imai, Department of Virology, Cancer Institute, Hokkaido Univ. School of Medicine, Kita 15, Nishi 7, Kita-ku, Sapporo 060, Japan
SOURCE: Gann Monographs on Cancer Research, (1998) 45/- (77-86).
Refs: 42
ISSN: 0072-0151 CODEN: GANMAX
COUNTRY: Japan
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
016 Cancer
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB An increasing number of surveys has documented that Epstein-Barr virus (EBV) **infection** is evident in cancerous lesions of primary gastric carcinomas. To verify the possible pathogenetic linkage of EBV with gastric carcinoma, detailed virological and immunological investigations were carried out on a large scale. A combination **screen** by EBV-encoded small RNA (EBER) in situ **hybridization** and polymerase chain reaction (PCR) revealed that 85 (7.1%) of 1,256 consecutive gastric carcinoma cases were positive for EBV. **Detection** of EBER and/or EBV-**determined** nuclear **antigen** (EBNA) 1 were strictly localized in all carcinoma cells, but were hardly present in normal mucosal epithelia or infiltrating leukocytes of individual tumors. The EBV genome existed in the tumor cells as a clonal episome unique

to each case. The results suggest that EBV is involved, not as a passenger, in the early phase of gastric carcinogenesis. EBV-carrying carcinoma cells expressed a restricted set of viral latent **genes**, similar to that of Burkitt's lymphoma cells. Patients with EBV-positive gastric carcinoma still sustained a level of EBV-specific **cytotoxic T-cell** response comparable to patients with EBV- negative gastric carcinoma and health controls. These findings lend support to the possibility that EBV-carrying gastric carcinoma cells can proliferate in the face of operative EBV-specific cellular immunity in vivo.

L10 ANSWER 31 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97368482 EMBASE
DOCUMENT NUMBER: 1997368482
TITLE: Nasal T/natural killer (NK)-cell lymphomas are derived from epstein- barr virus-infected cytotoxic lymphocytes of both NK- and T-cell lineage.
AUTHOR: Chiang A.K.S.; Chan A.C.L.; Srivastava G.; Ho F.C.S.
CORPORATE SOURCE: G. Srivastava, University Pathology Building, Queen Mary Hospital Compound, Pokfulam Road, Hong Kong, Hong Kong. sgopesh@hkucc.hku.hk
SOURCE: International Journal of Cancer, (1997) 73/3 (332-338).
Refs: 31
ISSN: 0020-7136 CODEN: IJCNAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The cellular nature of nasal T/natural killer (NK)-cell lymphomas (NLs) remains controversial. It is still debatable whether these represent T-cell lymphomas with extensive loss of surface **antigens** or are, in fact, true NK- cell lymphomas. They are associated closely with Epstein-Barr virus (EBV), to the extent that EBV-encoded small non-polyadenylated RNAs (EBER) expression can be used as a marker for the neoplastic cells. The cell lineage of this group of lymphomas was examined further by correlating immunophenotype, genotype and EBV status with the expression of cytotoxic granule-associated proteins, perforin and T-cell intracellular **antigen**-1 (TIA-1) in 13 cases of NL. Combined immunophenotypic and **gene** rearrangement analyses demonstrated that NLs can be **identified** clearly as either NK-cell or T-cell tumours. Nasal NK-cell lymphomas lacked clonal rearrangement of both T-cell receptor (TCR) .gamma. and immunogloulin heavy chain (IgH) **genes** and were either CD3(Leu4)- CD56+ (8 cases) or CD3(Leu4)+CD56+ (2 cases), whereas nasal T-cell lymphomas had rearranged TCR.gamma. and germ-line IgH **genes** and were either CD3(Leu4)+CD56+ (2 cases) or CD3(Leu4)+CD56- (I case). Immunohistochemical (IH) studies showed that both perforin and TIA-I were expressed universally in NL, irrespective of NK- or T-cell lineage. Dual labelling of TIA-I by IH and EBER by in situ **hybridisation** demonstrated that the granule proteins were expressed predominantly by the EBER+ tumour cells. Our results indicate that NLs are derived from EBV-infected cytotoxic lymphocytes of both NK- and T-cell lineage. We postulate that cytotoxic lymphocytes generated during the cellular immune

response to EBV **infection** or re-activation at the nasal region themselves may become targets for EBV **infection** and subsequent transformation.

L10 ANSWER 32 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97204170 EMBASE
DOCUMENT NUMBER: 1997204170
TITLE: Classification of T-cell and NK-cell neoplasms based on the REAL classification.
AUTHOR: Jaffe E.S.; Krenacs L.; Raffeld M.
CORPORATE SOURCE: Dr. E.S. Jaffe, Building 10, MSC-1500, 10 Center Drive, Bethesda, MD 20892-1500, United States
SOURCE: Annals of Oncology, (1997) 8/SUPPL. 2 (S17-S24). Refs: 77
ISSN: 0923-7534 CODEN: ANONE2
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Mature or peripheral T-cell lymphomas are uncommon, accounting for only 10%-15% of all non-Hodgkin's lymphomas. The classification of these neoplasms has been controversial. In contrast to B-cell lymphomas, cytologic grade has not been very useful in predicting the clinical course. This finding may result from the generally aggressive clinical course associated with T-cell lymphomas. Prior studies have suggested that stage of disease may be more important than cytologic subtype. Clinical presentation is very important in the classification of T-cell malignancies. For T-cell lymphomas, cytologic features alone are not sufficient to distinguish among disease entities. For example, adult T-cell leukemia/lymphoma (ATLL) often cannot be distinguished morphologically from **HTLV** -1-negative T-cell lymphomas. Most extranodal T- cell lymphomas appear to be derived from **cytotoxic T cells**, which express perforin, TIA-1, and granzyme B. Three broad groups of T-cell malignancies can be **identified**: (1) leukemic or systemic disease; (2) nodal disease; (3) extranodal disease. Anaplastic large-cell lymphoma (ALCL) is probably the single most common subtype of T-cell lymphoma. Classical ALCL should be distinguished from primary cutaneous ALCL (CD30+ lymphoproliferative disease of the skin), which is a distinct disease entity.

L10 ANSWER 33 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97183606 EMBASE
DOCUMENT NUMBER: 1997183606
TITLE: Regression of papillomas induced by cottontail rabbit papillomavirus is associated with infiltration of CD8+ cells and persistence of viral DNA after regression.
AUTHOR: Selvakumar R.; Schmitt A.; Iftner T.; Ahmed R.; Wettstein F.O.
CORPORATE SOURCE: F.O. Wettstein, Dept. of Microbiology/Immunology, UCLA School of Medicine, 10833 Le Conte Ave., Los

Angeles, CA 90095-1747, United States
SOURCE: Journal of Virology, (1997) 71/7 (5540-5548).
Refs: 51
ISSN: 0022-538X CODEN: JOVIAM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
016 Cancer
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Cottontail rabbit papillomavirus (CRPV) is a highly oncogenic papillomavirus and has been successfully used as a model to develop protective vaccines against papillomaviruses. Papillomas induced by the virus may spontaneously regress, suggesting that CRPV can also serve as a model to develop **therapeutic** vaccines. As a first step toward this goal, we have analyzed immunologic and viral aspects associated with papilloma regression and have **identified** several features unique to regression. Immunohistochemical staining of biopsies from growing and regressing papillomas and from sites after complete regression showed infiltration of CD8+ cells into the basal and suprabasal layers of the epidermis only during active regression. In situ **hybridizations** with mRNA-specific probes were strongly positive for E6 and E7 mRNAs during regression, but no late mRNA was present. Viral DNA was **detected** by in situ **hybridization** during regression but not after regression. However, analysis by PCR revealed persistence of viral DNA for several months at the majority of regression sites. The results suggest that stimulation of a strong CD8+ response to virus-infected cells is important for an effective **therapeutic** vaccine and that special attention should be given to the suppression of latent **infection**.

L10 ANSWER 34 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96082888 EMBASE
DOCUMENT NUMBER: 1996082888

TITLE: Characterization of Epstein-Barr virus-infected cells in benign lymphadenopathy of patients seropositive for **human** immunodeficiency **virus**.

AUTHOR: Brousset P.; Schlaifer D.; Roda D.; Massip P.; Marchou B.; Delsol G.
CORPORATE SOURCE: Laboratoire d'Anatomie Pathologique, Centre Hosp. Universitaire de Purpan, Place du Docteur Baylac,31059 Toulouse Cedex, France

SOURCE: Human Pathology, (1996) 27/3 (263-268).
ISSN: 0046-8177 CODEN: HPCQA4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The authors investigated 25 benign lymph nodes in patients infected with the **human** immunodeficiency **virus** (**HIV**) by in situ **hybridization** (ISH) and immunohistochemistry (IHC) to **detect** and characterize the Epstein-Barr virus (EBV)-infected cells. After ISH, 22 lymph nodes were found to contain various numbers of Epstein-Barr-encoded RNA

(EBER)-positive cells. Most of these cells were B cells. In six lymph nodes with numerous EBV-infected cells, EBNA2-positive/LMP1-positive lymphoblastoid cells were **detected** by IHC. Exceptional cells (in two specimens) were positively labeled with anti-Z Epstein-Barr replicative activator (ZEBRA) antibody or BamHI Left Frame 1/Not I (BHLF1/Not I) probes, indicating that EBV replication is not enhanced in the lymphocytes. In normal conditions (healthy individuals), small lymphocytes that express a restricted pattern of viral **genes** do escape immune response, whereas lymphoblastoid cells do not. Thus, impaired immune system may account for the late proliferation of lymphoblastoid cells (Epstein-Barr nuclear **antigen** [EBNA]2 positive/latent membrane protein [LMP]1 positive) in **HIV**-infected patients, and could explain why EBV-driven, **acquired** immunodeficiency **syndrome** (**AIDS**)-related, non-Hodgkin's lymphoma occur more frequently in patients with low CD4-positive T cells.

L10 ANSWER 35 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94349090 EMBASE
DOCUMENT NUMBER: 1994349090
TITLE: Induction by concanavalin A of specific mRNAs and cytolytic function in a CD8-positive T cell hybridoma.
AUTHOR: Jing Ji Gu; Harriss J.V.; Ozato K.; Gottlieb P.D.
CORPORATE SOURCE: Department of Microbiology, University of Texas,Austin, TX 78712, United States
SOURCE: Journal of Immunology, (1994) 153/10 (4408-4417). ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A previous report from this laboratory described the production of CD8+, class I-specific T cell hybridomas which developed specific cytolytic activity and the ability to secrete IL-2 upon Con A or specific Ag stimulation. Unlike normal lymphocytes or long-term **CTL** lines for which exposure to Ag triggers both differentiation and proliferation, T cell hybridoma lines can be activated functionally against a background of continuous proliferation. They therefore provide a unique system with which to study the molecular events involved in the induction of cytolytic function. The expression of mRNA from a series of **genes** was evaluated by Northern **hybridization** at various times after Con A stimulation of the H- 2L(d)-specific CD8+ 3D9 hybridoma. Induction of the c-fos proto-oncogene by 45 min poststimulation was followed shortly by c-myc induction. Perforin mRNA was expressed at a low level in the unstimulated hybridomas, but was down- regulated upon Con A stimulation to levels undetectable by PCR. Interestingly, production of granzyme A mRNA was strongly induced by 45 min after Con A stimulation. In the CD8+ RT-1.3G3 hybridoma, which is nonlytic and specific for the **HIV**-1 envelope glycoprotein, c-fos but not granzyme A mRNA was induced by 45 min poststimulation, and no granzyme A mRNA was **detectable** at any time. Thus, a significant role for granzyme A in the induction of cytolytic activity is suggested. Cytolysis by the 3D9 hybridoma involved both

target cell membrane damage and DNA fragmentation, and both Ca2+-dependent and Ca2+-independent cytolysis were observed. Although TNF-.alpha. mRNA was induced by 4 h poststimulation, Ab to TNF-.alpha. failed to inhibit the Ca2+-independent lysis observed, leaving the basis for the observed Ca2+-independent lysis unexplained.

L10 ANSWER 36 OF 53 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92289078 EMBASE
DOCUMENT NUMBER: 1992289078
TITLE: **Cytotoxic T lymphocytes** show HLA-C-restricted recognition of EBV-bearing cells and allorecognition of HLA class I molecules presenting self-peptides.
AUTHOR: Schendel D.J.; Reinhardt C.; Nelson P.J.; Maget B.; Pullen L.; Bornkamm G.W.; Steinle A.
CORPORATE SOURCE: Institute of Immunology, University of Munich, Goethestrasse 31,D-8000 Munich 2, Germany
SOURCE: Journal of Immunology, (1992) 149/7 (2406-2414). ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Human **CTL** have been isolated that show self-restricted recognition of autologous lymphoblastoid cell lines and allorecognition. The lymphoblastoid cell line ligand most likely used a peptide that is expressed in EBV-bearing cells when the virus enters the lytic cycle. This peptide is presented to CD8+ **CTL** by HLA-Cw7 molecules. The allogeneic ligand recognized on non-EBV- infected cells is composed of a class I glycoprotein and a naturally selected self-peptide. In previous studies we demonstrated that this ligand is **determined** by two MHC-linked **genes**: one **gene** encodes the allogeneic class I molecule whereas the other controls the self-peptide. Despite the use of different peptides and different class I molecules, seemingly equivalent structures are formed that enable these two ligands to function as **antigenic** mimics of each other. **CTL** with the same patterns of dual specificity could be isolated from four unrelated donors, indicating that HLA-Cw7 is frequently involved in self-restricted recognition of EBV-harboring cells. Such **CTL** could help not only to contain lytic virus during a primary **infection** but also may be maintained life-long to eliminate cells in which reactivated virus appears.

L10 ANSWER 37 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-315804 [35] WPIDS
DOC. NO. CPI: C2002-092032
TITLE: **Screening** for **therapeutics** (e.g. **antigens** for use in vaccines) for **infectious** diseases such as viral **infections**, by **identifying** immunogenic host cell **gene** products which are upregulated or expressed only during **infection**.

DERWENT CLASS: B04 D16
INVENTOR(S): ZAUDERER, M
PATENT ASSIGNEE(S): (UYRP) UNIV ROCHESTER
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002027027	A2	20020404	(200235)*	EN	42

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002027027	A2	WO 2001-US30334	20011001

PRIORITY APPLN. INFO: US 2000-236381P 20000929
AN 2002-315804 [35] WPIDS
AB WO 200227027 A UPAB: 20020603
NOVELTY - A new method (M1) for **screening** for **therapeutics** for **infectious** diseases, comprising **identifying** host cell **gene** products which are upregulated or expressed only during **infection**, **screening** the products for immunogenicity and **determining** which products are immunogenic.
ACTIVITY - Immunostimulant; antibacterial; antiparasitic; antiviral; antifungal.
No suitable biological data given.
MECHANISM OF ACTION - Vaccine.
No suitable biological data given.
USE - The method is useful for **screening** for **therapeutics** (e.g. **antigens** for use in vaccines) for **infectious** diseases such as viral, fungal, bacterial or parasitic **infections**.
Dwg.0/1

L10 ANSWER 38 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-239252 [29] WPIDS
DOC. NO. CPI: C2002-072121
TITLE: Representational Difference Analysis method for **identification** of **antigens** recognized by **cytotoxic T cells** and specific for human tumors, comprises improved selection of **genes** encoding target **antigens**.
DERWENT CLASS: B04 D16
INVENTOR(S): ZAUDERER, M
PATENT ASSIGNEE(S): (UYRP) UNIV ROCHESTER
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002018785	A1	20020214	(200229)*		54

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002018785	A1 Div ex	US 1997-935377	19970922
		US 2001-822250	20010402

PRIORITY APPLN. INFO: US 1997-935377 19970922; US 2001-822250 20010402

AN 2002-239252 [29] WPIDS

AB US2002018785 A UPAB: 20020508

NOVELTY - **Identifying** (M) a target epitope (I), comprising **screening** products of an expression library generated from DNA/RNA of a cell (C1) expressing (I) with **cytotoxic T cells** (C2) generated against C1 to **identify** DNA clones expressing (I), or providing C2 specific for a **gene** product differentially expressed by C1 and measuring cross-reactivity of C2 for C1 in which (I) is **identified** as a **gene** product inducing C2, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a viral vector (II) containing a DNA insert flanked by unique sites for restriction enzymes positioned so that religation of the viral vector arms is prevented and the orientation of the insert DNA is fixed and the DNA insert is operatively associated with a strong regulatory element.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Vaccine. No supporting data given.

USE - (M) is useful for **identifying** a target epitope or **antigen** specific for a tumor cell (claimed). (I) is also useful for **identifying** target **antigens** in other target cells against which it is desirable to induce cell-mediated immunity. The **antigen identified** by (M) is useful in vaccine preparations. (II) is useful for **treating** tumor-bearing mammals, including humans to generate immune response against the tumor cells. (II) is also useful for immunizing or vaccinating tumor-free subjects to prevent tumor formation.

ADVANTAGE - The method can **identify** potential **antigens** that are expressed not only by the pathogen, but also by the host cell whose **gene** expression is altered as a result of **infection**. Since many pathogens elude immune surveillance by frequent reproduction and mutation, the method is of considerable value to develop a vaccine that targets host **gene** products that are not likely to be subject to mutation.

DESCRIPTION OF DRAWING(S) - The figure shows the schematic of polymerase chain reaction SELECT method of Representational Difference Analysis.

Dwg.3/14

L10 ANSWER 39 OF 53 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-188381 [24] WPIDS

DOC. NO. CPI: C2002-058183

TITLE: New isolated or recombinant promoter/enhancers, useful in producing a prophylactic or **therapeutic** effect in humans, especially useful in **gene therapy** for **treating** or preventing **infectious** diseases, autoimmune disorders or tumors.

DERWENT CLASS: B04 D16

INVENTOR(S): PUNNONEN, J; SEMYONOV, A; WRIGHT, A

PATENT ASSIGNEE(S): (MAXY-N) MAXYGEN INC

COUNTRY COUNT: 95

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002000897	A2	20020103	(200224)*	EN	119
AU 2001068716	A	20020108	(200235)		

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002000897	A2	WO 2001-US20123	20010621
AU 2001068716	A	AU 2001-68716	20010621

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001068716	A	Based on	WO 200200897

PRIORITY APPLN. INFO: US 2000-213829P 20000623

AN 2002-188381 [24] WPIDS

AB WO 200200897 A UPAB: 20020416

NOVELTY - An isolated or recombinant nucleic acids, which comprise any of 18 sequences fully defined in the specification, is new. The nucleic acids are designated 10B2, 11E2, 12C9, 12E1, 12H9, 3C9, 4B5, 6A8, 6B2, 6D4, 6F6, 9E1, 9F11, 9G11, 9G12, 9G4, 9G7 and 9G8, and comprise 898-1768 base pair sequences.

DETAILED DESCRIPTION - An isolated or recombinant nucleic acids comprise a polynucleotide sequence:

(a) consisting of any of the 18 sequences, designated 10B2, 11E2, 12C9, 12E1, 12H9, 3C9, 4B5, 6A8, 6B2, 6D4, 6F6, 9E1, 9F11, 9G11, 9G12, 9G4, 9G7 or 9G8, or their complementary polynucleotide sequence;

(b) that has at least 97 % sequence identity to at least one sequence of (a);

(c) that has at least 80 % sequence identity to at least one sequence from (a), where the polynucleotide sequence promotes expression of an operably linked transgene at a level that is greater than the level of expression of the same transgene when operably linked to a human cytomegalovirus (CMV) promoter

polynucleotide sequence;

(d) comprising a fragment of (a)-(c), where the fragment promotes expression of an operably linked transgene at a level that is greater than the level of expression of the same transgene when operably linked to a human CMV promoter polynucleotide sequence;

(e) comprising a fragment of one sequence from (a), where the fragment comprises a unique subsequence; or

(f) that **hybridizes** under highly stringent conditions over substantially the entire length of (a)-(e).

INDEPENDENT CLAIMS are also included for the following:

(1) a method of producing a polypeptide, comprising:

(a) providing a population of cells comprising the nucleic acid operably linked to a transgene encoding a polypeptide; and

(b) expressing the polypeptide in at least the subset of the population of cells or their progeny;

(2) a method of producing a modified or recombinant nucleic acid by mutating or recombining the nucleic acids;

(3) a nucleic acid library produced by the method of (2), or comprising two or more of the novel nucleic acids;

(4) a vector comprising at least one of the novel nucleic acids;

(5) a cell comprising the novel nucleic acid or the vector of (4);

(6) a population of cells comprising the library of (3);

(7) compositions produced by:

(a) the cleaving of one or more of the novel nucleic acids, where the cleaving comprises mechanical, chemical or enzymatic cleavage; or

(b) by incubating one or more of the novel nucleic acids in the presence of deoxyribonucleotide triphosphates and a nucleic acid polymerase;

(8) compositions comprising the novel nucleic acids or the vector of (3), and a carrier;

(9) kits comprising the novel nucleic acid or the vector of (3);

(10) database comprising one or more character strings corresponding to:

(a) any of the novel nucleic acids; or

(b) a unique subsequence of the polynucleotide sequence of (a) or a unique subsequence of a complementary polynucleotide sequence of them; and

(11) methods for manipulating a sequence record in a computer system comprising:

(a) reading a character string corresponding to the novel nucleic acid;

(b) performing an operation on the character string; and

(c) returning a result of the operation.

ACTIVITY - Immunomodulator; Cytostatic; Antibacterial.

No biological data is given.

MECHANISM OF ACTION - Gene therapy; DNA vaccine.

USE - The nucleic acids are useful in producing an immunogenic effect, a prophylactic effect or a therapeutic effect in a subject, particularly a human (claimed). The nucleic acids are particularly useful in genetic (DNA) vaccination or gene therapy, e.g. for treating or preventing infectious diseases, autoimmune disorders or tumors. The nucleic acids are also useful for directing gene expression, particularly the levels of gene expression, in mammalian cells. The nucleic acids may also be used for producing any

polypeptide of interest for research, medical or industrial use. Dwg.0/10

L10 ANSWER 40 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-179901 [23] WPIDS
DOC. NO. CPI: C2002-055975
TITLE: Novel compositions comprising Chlamydia Cap1 protein and its use in the **treatment** of Chlamydia **infection**.
DERWENT CLASS: B04 D16
INVENTOR(S): BHATIA, A; FLING, S P; PROBST, P; SKEIKY, Y A W
PATENT ASSIGNEE(S): (CORI-N) CORIXA CORP
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002008267	A2	20020131	(200223)*	EN	526

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001080702 A 20020205 (200236)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002008267	A2	WO 2001-US23121	20010720
AU 2001080702	A	AU 2001-80702	20010720

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001080702	A	Based on	WO 200208267

PRIORITY APPLN. INFO: US 2001-841132 20010423; US 2000-620412 20000720
AN 2002-179901 [23] WPIDS
AB WO 200208267 A UPAB: 20020411
NOVELTY - Novel compositions comprising a Chlamydia Cap1 protein and methods for the diagnosis and **therapy** of Chlamydia **infection**.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a composition (C1) for eliciting an immune response comprising a Chlamydia Cap1 protein or an immunogenic fragment and an immunostimulant;

(2) a composition (C2) for eliciting an immune response comprising an isolated polynucleotide that encodes a Chlamydia Cap1 protein or an immunogenic fragment and an immunostimulant;

(3) a method (M1) for stimulating a Chlamydia-specific T-cell response and/or inhibiting the development of a Chlamydia **infection** in an animal, comprising administering (C1) or

(C2);

(4) an isolated polynucleotide (I) comprising a sequence selected from:

(a) four fully defined sequences (S1) of 1248, 1311, 813 and 750 base pairs given in the specification;

(b) complements of (S1);

(c) sequences consisting of at least 20 contiguous residues of (S1);

(d) sequences that **hybridize** to (S1), under highly stringent conditions;

(e) sequences that have at least 95%, preferably 99% identity to one of (S1); and

(f) degenerate variants of (S1);

(5) an isolated polypeptide (II) comprising an amino acid sequence selected from:

(a) sequences encoded by (I);

(b) sequences having at least 95%, preferably 99% identity to (II)

(6) an isolated polypeptide (III) comprising at least an immunogenic fragment of a polypeptide sequence selected from:

(a) four fully defined sequences (S2) of 412, 433, 264 and 249 amino acid residues given in the specification;

(b) a polypeptide sequence having at least 95%, preferably 99% identity to one of (S2);

(7) an expression vector (IV) comprising (I) operably linked to an expression control sequence;

(8) a host cell transformed or transfected with (IV);

(9) an isolated antibody or **antigen**-binding fragment that specifically binds to (II) and (III);

(10) a method (M2) for **detecting** the presence of Chlamydia in a patient;

(11) a fusion protein comprising (II) or (III);

(12) an oligonucleotide that **hybridizes** to one of (S1);

(13) a method (M3) for stimulating and/or expanding T cells specific for a Chlamydia protein, comprising contacting the T cells with at least one component;

(14) an isolated T cell population, comprising T cells prepared according to (M3);

(15) a composition (C3) comprising a first compound selected from physiologically acceptable carriers and immunostimulants and a second group;

(16) a method (M4) of stimulating an immune response in a patient, comprising administering a composition;

(17) methods (M5) for the **treatment** of Chlamydia **infection** in a patient;

(18) method (M6) for determining the presence of Chlamydia in a patient; and

(19) a diagnostic kit comprising at least one oligonucleotide that hybridizes to one of (S1).

ACTIVITY - Antibacterial; immunostimulant.

C3H mice (4 mice per group) were immunized three times with 50 micro g of pcDNA-3 expression vector containing C. trachomatis SWIB DNA (a fully defined 481 base pairs sequence and its corresponding 86 amino acid sequence protein given in the specification) encapsulated in poly lactitide co-glycolide microspheres (PLG); immunizations were made intra-peritoneally. Two weeks after the last immunization, animals were progesterone treated and infected by

inoculation of C. pisttaci in the vagina. Two weeks after the infection, mice were sacrificed and genital tracts sectioned, stained and examined for histopathology. Inflammation level was scored from mild (+) to very severe (+++++). Scores attributed to each single oviduct/ovary were summed and divided by the number of examined organs to get a mean inflammation for the group. Negative control-immunized animals receiving a PLG-encapsulated empty vector showed consistent inflammation with an ovary/oviduct mean inflammation score of 7.28, versus 5.71 for the PLG-encapsulated DNA immunized group. Inflammation in the peritoneum was 1.75 for the vaccinated group versus 3.75 for the control.

MECHANISM OF ACTION - Vaccine.

USE - C1 and C2 are useful for eliciting an immune response, specifically stimulating a Chlamydia-specific T-cell response or inhibiting the development of a Chlamydia infection in an animal. (M2) is useful for detecting the presence of Chlamydia in a patient and (M3) can be used to stimulate and/or expand T cells specific for a Chlamydia protein. (M5) are useful for treatment of a Chlamydia infection (claimed).

Dwg.0/12

L10 ANSWER 41 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-122061 [16] WPIDS
DOC. NO. NON-CPI: N2002-091568
DOC. NO. CPI: C2002-037377
TITLE: **Screening** assays for **identifying** compounds useful for **treating** immune disorders, comprises **identification** of compounds that modulate alpha 2-macroglobulin receptor-heat shock protein interaction.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): SRIVASTAVA, P K
PATENT ASSIGNEE(S): (UYCO-N) UNIV CONNECTICUT HEALTH CENT
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001092474	A1	20011206	(200216)*	EN	236
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR					
W: AU CA JP					
AU 2001075205	A	20011211	(200225)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001092474	A1	WO 2001-US18041	20010604
AU 2001075205	A	AU 2001-75205	20010604

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001075205	A Based on	WO 200192474

PRIORITY APPLN. INFO: US 2000-750972 20001228; US 2000-209095P 20000602; US 2000-625137 20000725; US

Searcher : Shears 308-4994

2000-668724 20000922

AN 2002-122061 [16] WPIDS

AB WO 200192474 A UPAB: 20020308

NOVELTY - **Screening** assays (M1) comprising **identification** of compounds that modulate alpha 2-macroglobulin (alpha 2M) receptor (which also functions as heat shock protein (HSP) receptor)-HSP interaction, is new.

DETAILED DESCRIPTION - M1 comprises:

(a) **identifying** (I) a compound that modulates an HSP-alpha 2M receptor-mediated process, by contacting a test compound with HSP and alpha 2M receptor or alpha 2M receptor-expressing cell, and measuring the level of alpha 2M receptor activity or expression, such that if the level of activity or expression measured in the presence of the compound differs from the level of alpha 2M receptor activity in the absence of the test compound, then a compound that modulates an HSP- alpha 2M receptor-mediated process is **identified;**

(b) **identifying** (II) a compound that modulates the binding of HSP to alpha 2M receptor, by contacting HSP with alpha 2M receptor, its fragment, analog, derivative or mimetic, in the present of a test compound and measuring the amount of HSP bound to alpha 2M receptor, its fragment, analog, derivative or mimetic, such that if the amount of bound HSP measured in the presence of the test compound differs from the amount of bound HSP measured in the absence of the test compound, then a compound that modulates the binding of an HSP to the alpha 2M receptor is **identified;**

(c) **identifying** (III) a compound that modulates HSP-mediated **antigen** presentation by alpha 2M receptor-expressing cells, by adding a test compound to a mixture of alpha 2M receptor expressing cells and a complex consisting essentially of HSP non-covalently associated with an **antigenic** molecule, under conditions conducive to alpha 2M receptor-mediated endocytosis, measuring the level of stimulation of **antigen**-specific **cytotoxic T cells** by alpha 2M receptor-expressing cells, such that if the level measured in the presence of the test compound differs from the level of the stimulation in the absence of the test compound, then a compound that modulates HSP-mediated **antigen** presentation by alpha 2M receptor-expressing cells is **identified;**or

(d) **detecting** (IV) a HSP- alpha 2M receptor-related disorder in a mammal, by measuring the level of activity from an HSP- alpha 2M receptor-mediated process in a patient sample, such that if the measured level differs from the level found in clinically normal individuals, then a HSP- alpha 2M receptor-related disorder is **detected.**

INDEPENDENT CLAIMS are also included for the following:

(1) modulating (M2) an immune response, by administering to a mammal a purified compound that modulates the interaction of HSP with alpha 2M receptor;

(2) **treating** (M3) an autoimmune disorder, by administering to a mammal in need of such **treatment** a purified compound that interferes with the interaction of HSP with the alpha 2M receptor;

(3) **treating** an autoimmune disorder, by administering to a mammal in need of such **treatment**, a recombinant cell that expresses an alpha 2M receptor which decreases the uptake of HSP by a functional alpha 2M receptor;

(4) increasing the immunopotency of a cancer cell or an infected cell;

(5) increasing the immunopotency of a cancer cell or an infected cell, by transforming the cell with a nucleic acid comprising a nucleotide sequence that is operably linked to a promoter, and encodes an alpha 2M receptor polypeptide, and administering the cell to individual in need of **treatment**, so as to obtain an elevated immune response;

(6) a recombinant cancer cell or recombinant infected cell (V) transformed with (N);

(7) a kit (K1);

(8) a kit (K2), in one or more containers;

(9) **identifying** an alpha 2M receptor fragment capable of binding HSP, by contacting HSP or its peptide-binding fragment with one or more alpha 2M receptor fragments, and **identifying** an alpha 2M receptor fragment which specifically binds to HSP or its peptide-binding fragment;

(10) **identifying** (M4) an alpha 2M receptor fragment capable of inducing an HSP- alpha 2M receptor-mediated process, by contacting HSP with a cell expressing alpha 2M receptor fragment and measuring the level of alpha 2M receptor activity in the cell, such that if the level of HSP- alpha 2M receptor-mediated process or activity measured is greater than the level of alpha 2M receptor activity in the absence of the alpha 2M receptor fragment, then an alpha 2M receptor fragment capable of inducing an HSP- alpha 2M receptor-mediated process is **identified**;

(11) **identifying** HSP fragment capable of binding an alpha 2M receptor, by contacting an alpha 2M receptor with one or more HSP fragments and **identifying** HSP fragment which specifically binds to the alpha 2M receptor;

(12) **identifying** (M5) HSP fragment capable of inducing an HSP- alpha 2M receptor-mediated process;

(13) **identifying** (M6) a molecule that binds specifically to an alpha 2M receptor;

(14) **screening** for molecules that specifically bind to an alpha 2M receptor;

(15) **identifying** a compound that modulates the binding of an alpha 2M receptor ligand to the alpha 2M;

(16) **identifying** a compound that modulates the interaction between the alpha 2M receptor and an alpha 2M receptor ligand;

(17) **identifying** (M7) a compound that modulates **antigen** presentation by alpha 2M receptor-expressing cells;

(18) modulating an immune response, by administering to a mammal a purified compound that binds to the alpha 2M receptor;

(19) **treating** or preventing a disease or disorder, by administering to a mammal a purified compound that binds to the alpha 2M receptor;

(20) **treating** an autoimmune disorder, by administering to a mammal in need of such **treatment** a purified compound that binds to the alpha 2M receptor;

(21) stimulating (M8) an immune response in a patient, by administering to the patient blood which has been withdrawn from the patient and **treated** to remove an alpha 2M receptor ligand;

(22) stimulating (M9) an immune response in a patient, by removing alpha 2M receptor ligand from blood withdrawn from the patient, and returning at least a portion of the alpha 2M receptor ligand-depleted blood to the patient;

(23) stimulating (M10) an immune response in a patient, by withdrawing blood from the patient, removing alpha 2M receptor ligand from the blood and returning at least a portion of alpha 2M receptor ligand-depleted blood to the patient; and

(24) a kit (K3);

ACTIVITY - Immunosuppressive; antiinflammatory; cytostatic; virucide; antilipemic; nootropic; antidiabetic; osteopathic.

MECHANISM OF ACTION - Modulator of interaction between alpha 2M receptor and HSP (claimed). No supporting data given.

USE - The interaction between alpha 2M receptor and HSP is useful in screening assays for identifying compounds that modulate the interaction of alpha 2M receptor and HSP. The identified compounds are useful for treating an autoimmune disorder, disease or disorder involving disruption of antigen presentation or endocytosis or cytokine clearance or inflammation, proliferative disorder, viral disorder or other infectious diseases, hypercholesterolemia, Alzheimer's disease, diabetes or osteoporosis (claimed).

Dwg.0/14

L10 ANSWER 42 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-082990 [11] WPIDS
DOC. NO. CPI: C2002-025139
TITLE: New composition, useful for **treatment** and/or prophylaxis of cancer and tumor, comprises immunostimulatory molecule and animal cells cultured in presence of interferon to enhance **antigen** presenting function of the cells.
DERWENT CLASS: B04 D16
INVENTOR(S): RALPH, S J
PATENT ASSIGNEE(S): (MONU) UNIV MONASH
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001088097	A1	20011122	(200211)*	EN	127

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001058040 A 20011126 (200222)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001088097	A1	WO 2001-AU565	20010517
AU 2001058040	A	AU 2001-58040	20010517

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001058040	A	Based on	WO 200188097

PRIORITY APPLN. INFO: AU 2000-7553 20000517
AN 2002-082990 [11] WPIDS
AB WO 200188097 A UPAB: 20020215
NOVELTY - A composition of matter (I) comprising an immunostimulatory molecule and animal cells cultured in the presence of at least one interferon (IFN) for a time and under conditions sufficient to enhance the **antigen** presenting function of the cells, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) enhancing (M1) immunopotentiation of animal cells comprising:

(a) culturing animal cells expressing an immunostimulatory membrane molecule in the presence of at least one IFN for a time and under conditions sufficient to enhance the **antigen** presenting functions of the cells; or

(b) culturing animal cells in the presence of at least one IFN for a time and under conditions sufficient to enhance the **antigen** presenting functions of the cells, and combining the cells so cultured with an immunostimulatory molecule in soluble form;

(2) enhancing (M2) or otherwise improving the immunogenicity of an **antigen** comprising providing animal cells cultured in the presence of at least one IFN for a time and under conditions sufficient to enhance the **antigen** presenting functions of the cells and loading the **antigen** onto the IFN-**treated** animal cells;

(3) a composition of matter (II) for eliciting an immune response against a target **antigen**, comprises animal cells cultured in the presence of at least one IFN for a time under conditions sufficient to enhance the **antigen** presenting functions of the cells, where an **antigen** corresponding to target **antigens** has been loaded onto IFN-**treated** animal cells;

(4) a vaccine (III) for stimulating a host's immune system, comprises (I) or (II);

(5) a kit (IV) comprising (I);

(6) assessing (M3) the responsiveness of animal cells to **treatment** with at least one IFN comprising **detecting** in the animal cells the level and/or functional activity of a polypeptide involved in interferon signaling, a modulatory agent that modulates the polypeptide, or a downstream cellular target of the polypeptide, or the level of an expression product of a **genetic** sequence encoding the polypeptide, the modulatory agent or the downstream cellular target;

(7) use of a target cell (V) in an assay for **detecting** cytolytic activity of a **cytotoxic T lymphocyte** (**CTL**) for the target cell, where the target cell has been cultured in the presence of at least one IFN for a time and under conditions sufficient to enhance the **antigen** presenting function of the cell;

(8) **detecting** (M4) **CTL** mediated lysis of a target cell comprising providing a target cell in the presence of at least one IFN for a time and under conditions sufficient to enhance the **antigen** presenting functions of the target cells, contacting the target cell with a **CTL** that has cytolytic activity for the target cell and **detecting CTL**-mediated lysis of the target cell; and

(9) use of an **antigen** binding molecule that is immuno-interactive with a polypeptide or modulatory agent, or a **detector** polynucleotide or oligonucleotide that **hybridizes** to the expression product in a kit for assessing the responsiveness of animal cells to **treatment** with at least one IFN.

ACTIVITY - Cytostatic; antitumor; antibacterial; virucide; fungicide; protozoacide.

MECHANISM OF ACTION - Vaccine; enhancer of **antigen** presenting function of cells (claimed). Preclinical trials were conducted using immunopotentiating composition as a cancer vaccine. **Treatment** of cells with gamma interferon (IFN) for 72 hours and beta -IFN for 48 hours was shown to optimally induce increased levels of surface expression of major histocompatibility complex (MHC) class I on melanoma cells, particularly on human melanoma cells. Levels of intracellular adhesion molecule (ICAM)-1 and B7 **antigens** on the human cells were also elevated by IFN **treatment**. However, given the common loss of B7 expression on these cells, the immunopotentiating composition included transfection to express B7-1 **antigen**. The transfected B7 expressing murine melanoma cells were shown to be unaltered in their responses to the optimal IFN **treatment** showing similar strong inductions of MHC class I **antigen**. Results from studies with the B16 melanoma model showed that the expression of B7-1 and IFN **treatment** were important for producing CD8 positive **cytotoxic T lymphocytes** (**CTLs**) with potent cytolytic activity against B16 cancer cells and that these cells were capable of lysing target cells even though they did not express B7 **antigen**. Given the level of immunity shown to be induced by the B7Hi interferon **treated** B16 cells measured by cytotoxicity assay, the same cell preparations were tested for their ability to induce anti-cancer immunity in whole animals when injected as a vaccine. The protocol compared the use of B7Hi/B16 transfected cells to vaccination with wild type B16 cells. The cells were irradiated and cohorts of mice were vaccinated by intraperitoneal injection weekly for up to six weeks. Vaccinated mice were challenged at week 7 with an injection subcutaneously on the rear flank with 5 multiply 10 to the power of 5 B7Med B16 cells. The results showed that all twenty control animals receiving only the challenge cancer cells succumbed to a 2 cm tumor growth by day 38. However, mice vaccinated with the B7Hi interferon **treated** immunopotentiating composition produced the greatest resistance to the challenge with 90% surviving with no sign of tumor and continued to remain tumor free thereafter. Thus, it was concluded that the B7Hi/IFN **treated** immunopotentiating composition induced potent CD8 positive **CTL** responses and were capable of providing sufficient immunity to protect the majority of vaccinated mice from the cancer cells.

USE - (I) or (III) is useful for **treatment** and/or prophylaxis of a disease or condition, such as tumorigenesis, by administering (I) or (III) to the patient. (I) which comprises the soluble immunostimulatory molecule and the cultured animal cells is administered separately, sequentially or simultaneously to the patient (claimed). (I) or (V) is useful for **treatment** and/or prophylaxis of cancer. (I), (II) or (V) is useful for **treating** viral, bacterial, fungal and protozoal **infections**.

Dwg.0/15

(3) STIC STN Search Report
09/966746

L10 ANSWER 43 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-571181 [53] WPIDS
DOC. NO. CPI: C2000-170161
TITLE: Recombinant chimeric nucleic acids encoding retroviral gag-fusion partner fusion proteins for producing pseudovirions which are useful as vaccines for **treating** and preventing cancer and **acquired** immunodeficiency **syndrome** (**AIDS**).
DERWENT CLASS: B04
INVENTOR(S): GONDA, M A; TOBIN, G J
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6099847	A	20000808	(200053)*		29

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6099847	A	Provisional	US 1996-20463P	19960516
			US 1997-857385	19970515

PRIORITY APPLN. INFO: US 1996-20463P 19960516; US 1997-857385 19970515
AN 2000-571181 [53] WPIDS
AB US 6099847 A UPAB: 20001023
NOVELTY - A recombinant chimeric nucleic acid (I) comprising a retroviral gag sequence, a target nucleic acid sequence derived from a nucleic acid encoding a fusion partner selected from Env, an interleukin (IL), tumor necrosis factor (TNF), granulocyte macrophage stem cell factor (GM/SCF), a non-retroviral viral **antigen** and a cancer **antigen** and a frame-shift (fs) site, is new.

DETAILED DESCRIPTION - A recombinant chimeric nucleic acid (I) comprising a retroviral gag sequence, a target nucleic acid sequence derived from a nucleic acid encoding a fusion partner selected from Env, an interleukin (IL), tumor necrosis factor (TNF), granulocyte macrophage stem cell factor (GM/SCF), a non-retroviral viral **antigen** and a cancer **antigen** and a frame-shift (fs) site, is new. In (I) the gag and target sequences are transcribed from a single start site of transcription and are in different reading frames.

INDEPENDENT CLAIMS are also included for the following:

(1) a pseudovirion (II) comprising a retroviral gag protein and a fusion partner, where the fusion protein partner is present in a Gag-fs-fusion partner fusion protein;

(2) an immunogenic composition (III) comprising (II);

(3) a particulate vaccine (IV) comprising (II);

(4) a fusion protein (V) comprising a retroviral Gag sequence, a translation reading frame switching sequence and a fusion partner; and

(5) a method (VI) of making a pseudovirion comprising

expressing a nucleic acid encoding a Gag-fs-fusion partner fusion protein in a cell, where the cell translates the nucleic acid into a protein comprising a Gag sequence and another protein comprising a gag sequence and a fusogenic partner.

ACTIVITY - Cytostatic; Anti-**HIV** (**human** immunodeficiency **virus**).

MECHANISM OF ACTION - Vaccine. The effect of non-**infectious** virus-like particles (VLPs) produced by insect cell expression of the **HIV**-1 Gag precursor protein by recombinant baculovirus in generating an **HIV**-specific **cytotoxic T-lymphocyte** (**CTL**) response was studied. Balb/c mice were inoculated with 2 mu g of Gag or Gag-SU (Gag coding sequence containing gp120) VLPs in phosphate buffered saline (PBS). Three weeks following the inoculation, splenocyte cultures from the mice were pooled, stimulated in vitro and tested for lysis of Gag and Env target cells. Splenocytes from mice immunized with Gag-SU VLPs lyzed both Gag and Env targets.

USE - (II), (III) or (IV) is useful for eliciting a **cytotoxic T-lymphocyte** (**CTL**) response against Env but does not elicit antibodies against Env (claimed). Pseudovirions containing Gag and Env protein sequences are useful for **treating** and preventing virally-mediated diseases such as **AIDS** (**acquired** immune deficiency **syndrome**) and pseudovirions containing cancer protein sequences are useful for **treating** and preventing cancer. They are also useful in assays to **detect** antisera to **HIV** in an individual infected with **HIV**.

Dwg.0/3

L10 ANSWER 44 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-376533 [32] WPIDS
DOC. NO. NON-CPI: N2000-282704
DOC. NO. CPI: C2000-113935
TITLE: Novel method of **identifying** target epitopes or **antigens** specific for human tumors, cancers and infected cells involving **screening** expression library products of a cell expressing the target epitope.
DERWENT CLASS: B04 D16 P14
INVENTOR(S): ZAUDERER, M
PATENT ASSIGNEE(S): (UYRP) UNIV ROCHESTER
COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000028016	A1	20000518	(200032)*	EN	132
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9913977	A	20000529	(200041)		
EP 1137769	A1	20011004	(200158)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000028016	A1	WO 1998-US24029	19981110
AU 9913977	A	WO 1998-US24029	19981110
		AU 1999-13977	19981110
EP 1137769	A1	EP 1998-957808	19981110
		WO 1998-US24029	19981110

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9913977	A	Based on	WO 200028016
EP 1137769	A1	Based on	WO 200028016

PRIORITY APPLN. INFO: WO 1998-US24029 19981110
AN 2000-376533 [32] WPIDS
AB WO 200028016 A UPAB: 20000706
NOVELTY - **Identifying** (I) a target epitope (TE) comprising **screening** the products of an expression library from a cell (C) expressing TE, with **cytotoxic T cells** (**CTLs**) generated against the C to **identify** DNA clones expressing TE, or providing a **CTL** specific for a **gene** product (GP) differentially expressed by a C and measuring the cross-reactivity of the **CTL**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a viral vector (V) containing a DNA insert operably linked to a strong regulatory element and flanked by unique sites for restriction enzymes positioned so that religation of viral vectors arms is prevented and orientation of insert DNA is fixed;

(2) a transgenic animal (II) tolerized with a non-tumorigenic cell line that does not express co-stimulator activity; and

(3) a **CTL** derived from (II).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Vaccine.

Groups of 5 mice of the BALB/c strain syngeneic to the murine tumors were immunized with vaccinia virus recombinant for a full length cDNA differentially expressed in all four murine tumor lines but not the parental B/c.N cells. Each group of mice was assayed for induction of protective immunity by challenge with a tumorigenic inoculum of 1 multiply 106 BCA 39 tumor cells. Results not given.

USE - (I) is useful for **identifying** tumor specific target epitopes (TEs) (claimed) and **antigens** which are useful in immunogenic compositions or vaccines to induce the regression of tumors, cancers or **infections** in mammals including human. The **genes** expressed in a panel of tumor cells that are derived from single immortalized, non-tumorigenic cell line are used to generate HLA restricted **CTLs** which are evaluated for activity against tumor cells.

ADVANTAGE - (I) is useful for **identifying** target **antigens** in other target cells against which it is desirable to induce cell mediated immunity. The method is useful to **identify** potential **antigens** expressed not only by the pathogen but also by the host cells whose **gene** expression is altered as a result of **infection**. The

differential **gene** expression strategies can be applied to **identify** immunogenic molecules of cells infected with virus, fungus or mycobacterium.

DESCRIPTION OF DRAWING(S) - The diagram shows a schematic of the PCR Select (RTM) method of Representational Difference Analysis. Dwg.3/14

L10 ANSWER 45 OF 53 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-061918 [05] WPIDS
CROSS REFERENCE: 2000-271403 [23]; 2000-647065 [53]
DOC. NO. CPI: C2000-017064
TITLE: New human interleukin-17 receptor like protein, e.g. to **treat** disorders relating to cellular activation.
DERWENT CLASS: B04 D16
INVENTOR(S): RUBEN, S M; SHI, Y
PATENT ASSIGNEE(S): (HUMA-N) HUMAN GENOME SCI INC
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9914240	A1	19990325	(200005)*	EN	132
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9894824	A	19990405	(200005)		
EP 1015488	A1	20000705	(200035)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9914240	A1	WO 1998-US19121	19980916
AU 9894824	A	AU 1998-94824	19980916
EP 1015488	A1	EP 1998-948201	19980916
		WO 1998-US19121	19980916

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9894824	A	Based on	WO 9914240
EP 1015488	A1	Based on	WO 9914240

PRIORITY APPLN. INFO: US 1997-59133P 19970917
AN 2000-061918 [05] WPIDS
CR 2000-271403 [23]; 2000-647065 [53]
AB WO 9914240 A UPAB: 20001205
NOVELTY - Nucleic acid molecules (NAM's) encode human interleukin (IL)-17 receptor like protein (IL17RLP) (P1) and are obtained from a cDNA library of human adult pulmonary tissue.

DETAILED DESCRIPTION - (A) NAM has a polynucleotide (PN) having nucleotide (nt) sequence (NS) at least 95% identical to:

(a) NS encoding P1 having complete amino acid (aa) sequence (CAS) (I) (aa -19 to 407) of 426 aa (given in the specification);

(b) NS encoding P1 having CAS (I) except the N-terminal methionine (aa -18 to 407);

(c) NS encoding predicted mature P1 with a sequence at aa 1-407 in (I);

(d) NS encoding polypeptide (plp) comprising predicted extracellular domain (ED) of P1 having a sequence at aa 272-292 in (I);

(e) NS encoding soluble P1 with predicted ED and intracellular domains (**ID**), but lacking the predicted transmembrane domain (TD);

(f) NS encoding P1 having CAS encoded by cDNA clone (ATCC No. 209198);

(g) NS encoding P1 having CAS except N-terminal methionine encoded as in (f);

(h) NS encoding mature P1 having sequence encoded as in (f);

(i) NS encoding ED of P1 having sequence encoded as in (f), and

(j) NS complementary to NS' of (a)-(i).

INDEPENDENT CLAIMS are also included for the following:

(1) NAM comprising PN having NS at least 95% identical to:

(a) NS encoding plp with residues n-407 of (I), where n is an integer in the range of -19 to -5;

(b) NS encoding plp with residues -19-m of (I), where m is an integer in the range of 340-407;

(c) NS encoding plp having residues n-m of (I), where n and m are defined in (a) and (b);

(d) NS encoding plp having portion of CAS of IL17RLP encoded as in (Af), which excludes from 1-23 aa from the N-terminus of CAS encoded as in (Ag);

(e) NS encoding plp consisting of a portion of CAS of IL17RLP encoded as in (d), which excludes from 1-67 aa from the carboxy terminus of the CAS encoded as in (Ag), and

(f) NS encoding plp having a portion of CAS of IL17RLP encoded as in (d), which includes a combination of any of the N- and carboxy terminal deletions in (d) and (e);

(2) NAM comprising PN **hybridizing** to PN having NS identical (Aa)-(Aj), where the PN which **hybridizes** does not **hybridize** to PN having a NS with only A or T residues;

(3) NAM comprising PN encoding a sequence of an epitope-bearing portion of P1 having a sequence as in (Aa)-(Ai);

(4) making recombinant vector (RV) by inserting NAM of (A) into RV;

(5) RV produced by (4);

(6) making a recombinant host cell (RHC) by introducing RV of (5) into it;

(7) RHC produced by (6);

(8) P1 comprising an aa sequence at least 95% identical to:

(a) sequence of a full-length P1 having CAS (I) (aa -19 to 407);

(b) sequence of a full-length P1 having CAS (I) except the N-terminal methionine (aa -18 to 407);

(c) sequence of a mature P1 having CAS (I) (aa 1 to 407);

(d) sequence of predicted ED of P1 having a complete (I) (aa 1 to 271);

(e) sequence of a soluble P1 having predicted ED and ID, but lacking the predicted TD;

(f) CAS encoded as in (Ag);

(g) CAS except the N-terminal methionine encoded as in (Ag);
(h) CAS of a mature IL17RLP encoded as in (Af), and
(i) CAS of ED of an IL17RLP encoded as in (Ag);
(9) plp comprising an epitope-bearing portion of P1 which is selected from plp having aa's Ser-14 to Val-22, Cys-24 to Pro-32, Ile-41 to Arg-49, Thr-89 to Val-97, Thr-110 to Lys-118, Ala-144 to Ser-152, Thr-240 to Val-248, Gly-258 to Thr-267, Leu-280 to Gly-288, Cys-4004 to Glu-412, Pro-425 to Ser-423, Gly-409 to Glu-417, and Cys-404 to Leu-426 in (I);
(10) an antibody (Ab) specific for P1 of (8), and
(11) NAM comprising PN having a sequence at least 95% identical to NS of:
(a) (II) of 409 nt;
(b) (III) of 327 nt;
(c) a portion of (IV) of 1816 nt where the portion comprises at least 50 contiguous nt from nt 50-650;
(d) a portion of (IV) having nt's 50-1800, 100-1800, 200-1800, 400-1800, 500-1800, 600-1800, 50-650, 100-650, 200-650, 300-650, 400-650, 500-650, 50-500, 100-500, 200-500, 200-500, 300-500, 400-500, 50-400, 100-400, 200-400, 300-400, 50-300, 100-300, 200-300, 50-200, 100-200, and 50-100; and
(e) complementary to NSs in (a)-(d) (all sequences are given in the specification).

ACTIVITY - The IL17RLP activates signal transduction pathways resulting in stimulation of NF-kappaB transcription factor family, secretion of IL-6 and costimulation of T-cell proliferation, induction of IL-6, IL-8, G-CSF, prostaglandin E (PGE2) and intracellular adhesion molecule (ICAM-1) expression, regulation of hematopoietic stem and progenitor cell growth and expansion, myelosuppressive activity for stem and immature subsets of myeloid progenitors, activation and stimulation of hematopoiesis (neutrophil hematopoiesis), enhancement of erythropoiesis, suppression of lymphopoiesis and myelopoiesis and strong suppression of monocytopoiesis, antigenicity (ability to bind (or compete with P1 for binding) to anti-IL17RLP Ab), immunogenicity (ability to generate Ab to P1), the ability to form polymers with other P1 or P1-like polypeptides, and ability to bind to a receptor or ligand for P1.

USE - P1's and agonists can be used to treat disorders relating to cellular activation, hemostasis, angiogenesis, tumor metastasis, cellular migration and ovulation, and neurogenesis. They can also be used to enhance host defenses against resistant chronic and acute infections, e.g. mycobacterial infections via the attraction and activation of microbial leukocytes. IL17RLP may also be used to increase T-cell proliferation by the stimulation of IL-2 biosynthesis for the treatment of T-cell mediated autoimmune diseases and lymphocytic leukemias, to regulate hematopoiesis by regulating the activation and differentiation of various hematopoietic progenitor cells, e.g. to release mature leukocytes from the bone marrow following chenotherapy, i.e. in stem cell mobilization or to treat sepsis. The products can also be used for the diagnosis or treatment of immune system related disorders e.g. tumors, cancers, interstitial lung disease (such as Langehans cell granulomatosis), and any disregulation of immune cell function including autoimmunity, arthritis, leukemias, lymphomas, immunosuppression, immunity, humoral immunity, inflammatory bowel disease, or myelo suppression. Antagonists may be used to inhibit the activation of macrophages and their precursors, and of

neutrophils, basophils, B lymphocytes and some T-cell subsets, e.g. activated and CD8 cytotoxic T cells and natural killer cells, in certain auto-immune and chronic inflammatory and infective diseases, e.g. autoimmune diseases including multiple sclerosis and insulin-dependent diabetes, infectious diseases including silicosis, sarcoidosis, idiopathic pulmonary fibrosis by preventing the activation of mononuclear phagocytes, idiopathic hypereosinophilic syndrome by preventing eosinophil production, or rheumatoid arthritis by preventing the activation of monocytes in the synovial fluid in the joints of patients or to treat or prevent inflammation. Dwg.0/3

L10 ANSWER 46 OF 53 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2002:233020 SCISEARCH
THE GENUINE ARTICLE: 528QU
TITLE: A defective, rearranged Epstein-Barr virus genome in EBER-negative and EBER-positive Hodgkin's disease
AUTHOR: Gan Y J; Razzouk B I; Su T; Sixbey J W (Reprint)
CORPORATE SOURCE: Louisiana State Univ, Hlth Sci Ctr, Dept Microbiol & Immunol, 1501 Kings Highway, Shreveport, LA 71130 USA (Reprint); Louisiana State Univ, Hlth Sci Ctr, Dept Microbiol & Immunol, Shreveport, LA 71130 USA; Louisiana State Univ, Hlth Sci Ctr, Feist Weiller Canc Ctr, Shreveport, LA 71130 USA; St Jude Childrens Hosp, Memphis, TN USA
COUNTRY OF AUTHOR: USA
SOURCE: AMERICAN JOURNAL OF PATHOLOGY, (MAR 2002) Vol. 160, No. 3, pp. 781-786.
Publisher: AMER SOC INVESTIGATIVE PATHOLOGY, INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3993 USA.
ISSN: 0002-9440.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 45

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A ubiquitous herpesvirus that establishes life-long **infection**, the Epstein-Barr virus (EBV) has yielded little insight into how a single agent in general accord with its host can produce diverse pathologies ranging from oral hairy leukoplakia to nasopharyngeal carcinoma, from **infectious** mononucleosis to Hodgkin's disease (HD) and Burkitt's lymphoma. Its pathogenesis is further confounded by the less than total association of virus with histologically similar tumors. in other viral systems, defective (interfering) viral genomes are known to modulate outcome of **infection**, with either ameliorating or intensifying effects on disease processes initiated by prototype strains. To ascertain whether defective EBV genomes are present in HD, we examined paraffin-embedded tissue from 56 HD cases whose EBV status was first **determined** by cytohybridization for nonpolyadenylated EBV RNAs (EBERs). Using both standard polymerase chain reaction (PCR) and PCR in situ **hybridization**, we successfully amplified sequences that span abnormally juxtaposed BamHI W and Z fragments characteristic of defective heterogeneous (het) EBV DNA from 10 of 32 (31%) EBER-positive tumors. Of 24 EBER-negative HD, 8 yielded PCR products indicating presence of bet EBV DNA. Two of these contained defective EBV In the apparent absence of the prototype virus. Of the 42 tumors analyzed for defective EBV by both PCR techniques, there was concordance of results in 38 (90%). **Detection** of

defective EBV genomes with the potential to disrupt viral **gene** regulation suggests one mechanism for pathogenic diversity that may also account for loss of prototypic EBV from individual tumor cells.

L10 ANSWER 47 OF 53 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2001:459852 SCISEARCH
THE GENUINE ARTICLE: 437LL
TITLE: Rapid and wide-reaching delivery of **HIV**-1 env DNA vaccine by intranasal administration
AUTHOR: Tadokoro K; Koizumi Y; Miyagi Y; Kojima Y; Kawamoto S; Hamajima K; Okuda K (Reprint); Tanaka S; Onari K; Wahren B; Aoki I; Okuda K
CORPORATE SOURCE: Yokohama City Univ, Sch Med, Dept Bacteriol, Kanazawa Ku, 3-9 Fukuura, Yokohama, Kanagawa 2360004, Japan (Reprint); Yokohama City Univ, Sch Med, Dept Bacteriol, Kanazawa Ku, Yokohama, Kanagawa 2360004, Japan; Yokohama City Univ, Sch Med, Dept Internal Med, Yokohama, Kanagawa 2360004, Japan; Yokohama City Univ, Sch Med, Dept Pathol, Yokohama, Kanagawa 2360004, Japan; Tokyo Dent Coll, Dept Bacteriol, Mihama Ku, Masago, Japan; Yokohama Minami Kyosai Hosp, Dept Orthoped Surg, Yokohama, Kanagawa, Japan; Karolinska Inst, Swedish Inst Infect Dis Control, Stockholm, Sweden
COUNTRY OF AUTHOR: Japan; Sweden
SOURCE: VIRAL IMMUNOLOGY, (5 MAY 2001) Vol. 14, No. 2, pp. 159-167.
Publisher: MARY ANN LIEBERT INC PUBL, 2 MADISON AVENUE, LARCHMONT, NY 10538 USA.
ISSN: 0882-8245.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 41

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Although the potential of DNA vaccination is now beginning to be greatly appreciated, no detailed study of its localization in tissue or its expression kinetics has been reported. In this study, we investigated these issues using **HIV**-1 DNA plasmids administered either intranasally or intramuscularly, Fluorescence in situ **hybridization** (FISH) revealed that the **human** immunodeficiency **virus** (**HIV**) plasmids administered intranasally localized in the alveoli, lung, liver, spleen, regional lymph nodes, kidney, fetus, and esophagus, These **HIV** plasmids were **detected** 2 to 4 weeks after administration. We **detected** messenger RNA production of **HIV** env **gene** in the lung, liver and spleen, and **human** immunodeficiency **virus** type 1 (**HIV** -1)-specific proteins were **detectable** in the lung, These observations may provide important information for understanding the mechanisms of strong immune activation induced by DNA vaccination via the intranasal route. This technology of DNA administration suggests possible practical applications for vaccination and probably for **gene therapy**.

L10 ANSWER 48 OF 53 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2000:319248 SCISEARCH
THE GENUINE ARTICLE: 306TX

TITLE: DNA-based vaccination induces humoral and cellular immune responses against hepatitis B virus surface **antigen** in mice without activation of C-myc

AUTHOR: Zhao L S (Reprint); Qin S; Zhou T Y; Tang H; Liu L; Lei B J

CORPORATE SOURCE: W CHINA UNIV MED SCI, HOSP 1, DEPT INFECT DIS, CHENGDU 610041, PEOPLES R CHINA (Reprint); KEY LAB SICHUAN PROV MOL BIOL INFECT DIS, CHENGDU 610041, PEOPLES R CHINA

COUNTRY OF AUTHOR: PEOPLES R CHINA

SOURCE: WORLD JOURNAL OF GASTROENTEROLOGY, (APR 2000) Vol. 6, No. 2, pp. 239-243.
Publisher: W J G PRESS, PO BOX 2345, BEIJING 100023, PEOPLES R CHINA.
ISSN: 1007-9327.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 39

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB AIM To develop a safe and effective DNA vaccine for inducing humoral and cellular immunological responses against hepatitis B virus surface **antigen** (HBsAg).

METHODS BALB/c mice were inoculated with NV-HB/s, a recombinant plasmid that had been inserted S **gene** of hepatitis B virus genome and could express HBsAg in eukaryotes, HBsAg expression was measured by ABC immunohistochemical assay, generation of anti-HBs by ELISA and **cytotoxic T lymphocyte** (**CTL**), by MIT method, existence of vaccine DNA by Southern blot **hybridization** and activation of oncogene C-myc by in situ **hybridization.**

RESULTS With NV-HB/s vaccination by intramuscular injection, anti-HBs was initially positive 2 weeks after inoculation while all mice tested were HBsAg positive in the muscles. The titers and seroconversion rate of anti-HBs were steadily increasing as time went on and were dose-dependent. All the mice inoculated with 100 mu g NV-HB/s were anti-HBs positive one month after inoculation, the titer was 1:1024 or more. The humoral immune response was similar induced by either intramuscular or intradermal injection. **CTL** activities were much stronger (45.26%) in NV-HB/s DNA immunized mice as compared with those (only 6%) in plasma-derived HBsAg vaccine immunized mice. Two months after inoculation, all muscle samples were positive by Southern-blot **hybridization** for NV-HB/s DNA **detection**, but decreased to 25% and all were undetectable by in situ **hybridization** after 6 months, No oncogene C-myc activation was found in the muscle of inoculation site.

CONCLUSION NV-HB/s could generate humoral and cellular immunological responses against HBsAg that had been safely expressed in situ by NV-HB/s vaccination.

L10 ANSWER 49 OF 53 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1999:795521 SCISEARCH
THE GENUINE ARTICLE: 245NG
TITLE: Basis of rabies virus neurovirulence in mice: expression of major histocompatibility complex class I and class II mRNAs
AUTHOR: Irwin D J; Wunner W H; Ertl H C J; Jackson A C (Reprint)

CORPORATE SOURCE: QUEENS UNIV, KINGSTON GEN HOSP, DEPT MED, CONNELL 725, 76 STUART ST, KINGSTON, ON K7L 2V7, CANADA (Reprint); QUEENS UNIV, KINGSTON GEN HOSP, DEPT MED, KINGSTON, ON K7L 2V7, CANADA; QUEENS UNIV, DEPT MICROBIOL & IMMUNOL, KINGSTON, ON K7L 3N6, CANADA; WISTAR INST ANAT & BIOL, PHILADELPHIA, PA 19104
COUNTRY OF AUTHOR: CANADA; USA
SOURCE: JOURNAL OF NEUROVIROLOGY, (OCT 1999) Vol. 5, No. 5, pp. 485-494.
Publisher: STOCKTON PRESS, HOUNDMILLS, BASINGSTOKE RG21 6XS, HAMPSHIRE, ENGLAND.
ISSN: 1355-0284.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 49

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Expression of major histocompatibility complex (MHC) molecules on cells of the central nervous system (CNS) plays an important role in the pathogenesis of acute viral encephalitis. We have compared the induction of MHC class I and II mRNA transcripts in mice upon **infection** with the virulent challenge virus standard (CVS) strain of rabies virus and avirulent rabies virus variant RV194-2. Rabies virus **antigen** was **detected** with immunoperoxidase staining and S-35-labeled RNA probes were used to **detect** MHC class I and class II mRNA transcripts by in situ **hybridization** in infected brains. In CVS and RV194-2 infected animals, MHC class I mRNA expression occurred in the brain in neurons, glia, choroid plexus epithelial cells, ependymal cells, and inflammatory cells; expression was moderately higher in CVS-infected mice. In contrast, MHC class II mRNA expression was minimal in CVS-infected mice and it was markedly upregulated in CNS inflammatory cells upon RV194-2 **infection**. Both viruses induced an acute inflammatory reaction in the cerebrospinal fluid (CSF), which was more pronounced in CVS-infected mice. Both viruses also induced an **antigen** specific T and B cell response **detectable** in lymph nodes and spleen. These studies, which show a correlation between greater expression of MHC class II mRNA in the brain following intracerebral RV194-2 **infection** and protection against RV194-2 **infection** in the brain, suggest that recovery from avirulent rabies virus **infection** of neural cells involves T helper cells produced and/or retained in the brain for reasons that are not entirely clear.

L10 ANSWER 50 OF 53 SCISEARCH COPYRIGHT 2002 ISI (R)

ACCESSION NUMBER: 1999:550620 SCISEARCH
THE GENUINE ARTICLE: 214RX

TITLE: Effect of Epstein-Barr virus **infection** on response to chemotherapy and survival in Hodgkin's disease

AUTHOR: Murray P G (Reprint); Billingham L J; Hassan H T; Flavell J R; Nelson P N; Scott K; Reynolds G; Constandinou C M; Kerr D J; Devey E C; Crocker J; Young L S
CORPORATE SOURCE: WOLVERHAMPTON UNIV, SCH HLTH SCI, BIOMED RES LABS, DIV BIOMED SCI, WOLVERHAMPTON WV1 1DJ, W MIDLANDS, ENGLAND (Reprint); UNIV BIRMINGHAM, CRC, INST CANC STUDIES, BIRMINGHAM, W MIDLANDS, ENGLAND; NEW CROSS

HOSP, DEPT HISTOPATHOL, WOLVERHAMPTON, W MIDLANDS, ENGLAND; RUSSELLS HALL HOSP, DEPT HISTOPATHOL, DUDLEY, W MIDLANDS, ENGLAND; BIRMINGHAM HEARTLANDS HOSP, DEPT HISTOPATHOL, BIRMINGHAM B9 5ST, W MIDLANDS, ENGLAND
COUNTRY OF AUTHOR: ENGLAND
SOURCE: BLOOD, (15 JUL 1999) Vol. 94, No. 2, pp. 442-447. Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399. ISSN: 0006-4971.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 58

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have analyzed paraffin sections from 190 patients with histologically confirmed Hodgkin's disease (HD) for the presence of Epstein-Barr virus (EBV) using in situ **hybridization** to **detect** the EBV-encoded Epstein Barr virus early RNAs (EBERs) and immunohistochemistry to **identify** latent membrane protein-1 (LMP1) expression. EBV was present in the tumor cells in 51 HD cases (27%) and was mainly confined to the mixed cellularity and nodular sclerosis subtypes. There was no difference between EBV-positive and EBV-negative HD patients with regard to age, clinical stage, presentation, and the number of alternating chemotherapy cycles of ChIVPP and PABIOE received. The complete remission rate after study chemotherapy was 80% in EBV positive patients versus 69% in EBV-negative patients (P = .05). The 2-year failure-free survival rate was significantly better for EBV-positive patients when compared with the EBV-negative HD group (P = .02), Although 2-year and 5-year overall survival rates were better for EBV-positive HD patients, the differences were not statistically significant (P = .18 and P = .40, respectively). In conclusion, the results confirm the favorable prognostic value of EBV in the tumor cells of HD patients and suggest important differences in response to chemotherapy between EBV-positive and EBV negative patients. (C) 1999 by The American Society of Hematology.

L10 ANSWER 51 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 1000445529 JICST-EPlus
TITLE: A Histopathological Analysis of the Lymphoma-associated Hemophagocytic Syndrome. Re-Examination of Malignant Histiocytosis.
AUTHOR: MITSUTANI TOSHIYUKI; KISHIMOTO KOJI; SUZUKI TAKAO; TATE GENSHU
CORPORATE SOURCE: Showa Univ., Fujigaoka Hospital
SOURCE: Showa Igakkai Zasshi (Journal of the Showa Medical Association), (1999) vol. 59, no. 6, pp. 635-645. Journal Code: Z0096B (Fig. 10, Tbl. 5, Ref. 27) CODEN: SIGZAL; ISSN: 0037-4342
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

AB A malignant histiocytosis (MH) had been considered a main entity of the hemophagocytic syndrome (HPS), but as a result of advances in immunological and molecular biological diagnostic technology in the 1990s, many of the cases diagnosed as MH have been re-categorized as

non-Hodgkin's lymphoma.In 1984, we reported 8 cases which had been clinically diagnosed as so-called malignant reticulosis and subsequently diagnosed as MH based on the findings of postmortem examination. When we re-evaluated these 8 cases by various approaches which included immunohistochemical examinations against B, T/NK, histiocytic markers, cytotoxic molecules and oncogene products as well as in situ **hybridization** (ISH) to **detect** EB virus encoded small RNAs (EBER), it turned out that half of them were finally diagnosed as B-cell lymphoma and half as T-cell lymphoma; in addition, two cases of T cell lymphoma were cytotoxic lymphoma. It was reported that the extra-nodular NK/T cell lympoma was the major causes of LAHS, however, this study of 8 cases showed that lymphoma cells in all cases were negative for CD56, one of the NK cell marker. Analysis of the EBV **infection** by ISH indicated that the EBER-1 was **detected** only one case among 4 T cell-LAHS cases. (author abst.)

L10 ANSWER 52 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 960819478 JICST-EPlus
TITLE: **Infectious** diseases and test methods. EB virus **infectious** disease.
AUTHOR: KIKUTA HIDEAKI
CORPORATE SOURCE: Hokkaido Univ., Sch. of Med.
SOURCE: Kensa to Gijutsu (Modern Medical Laboratory), (1996) vol. 24, no. 7, pp. 223-226. Journal Code: Z0084B (Tbl. 2, Ref. 3)
ISSN: 0301-2611
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
STATUS: New
AB EB virus (I) is a common virus in humans. The majority of primary **infections** result in latent **infections**, however, sometimes the onset of **infectious** mononucleosis is observed.This paper explains diagnostic and test methods for I and other related diseases.Test methods include assays of I related antibody titer, **detection** of viral **antigen**, DNA and RNA, specific **cytotoxic T cell** activity of I and chromosomal analysis.

L10 ANSWER 53 OF 53 JICST-EPlus COPYRIGHT 2002 JST
ACCESSION NUMBER: 950712097 JICST-EPlus
TITLE: Segmented Filamentous Bacteria Are Indigenous Intestinal Bacteria That Activate Intraepithelial Lymphocytes and Induce MHC Class II Molecules and Fucosyl Asialo GM1 Glycolipids on the Small Intestinal Epithelial Cells in the Ex-Germ-Free Mouse.
AUTHOR: UMESAKI Y; OKADA Y; MATSUMOTO S; IMAOKA A; SETOYAMA H
CORPORATE SOURCE: Yakult Central Inst. Microbiological Res., Tokyo, JPN
SOURCE: Microbiol Immunol, (1995) vol. 39, no. 8, pp. 555-562. Journal Code: F0715A (Fig. 8, Ref. 29)
ISSN: 0385-5600
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
STATUS: New
In ex-germ-free mice conventionalized by association with fecal

microorganisms, the induction of major histocompatibility complex class II molecules and fucosylation of asialo GM1 glycolipid occur in the small intestinal epithelial cells (IEC). The intestinal intraepithelial lymphocytes (IEL), especially .ALPHA..BETA. T-cell receptor-bearing ones, also remarkably expand and show cytolytic activity. In this study, we investigated the immunological and physiological characteristics of the small intestine induced by a kind of indigenous bacteria of the small intestine, segmented filamentous bacteria (SFB), among chloroform-resistant intestinal bacteria. Monoassociation of SFB with germ-free mice was confirmed by the **determination** of the base sequences of polymerase chain reaction products of 16S rRNA **genes** of the fecal bacteria of these mice and in situ **hybridization** using fluorescein-labeled probes based on them. SFB increased the number of .ALPHA..BETA.TCR-bearing IEL and induced Thy-1 expression and cytolytic activity of IEL. The induction of MHC class II molecules and fucosyl asialo GM1 glycolipids and the increases in the mitotic activity and the ratio of the number of columnar cells to those of goblet cells also occurred in the small intestinal epithelial cells on monoassociation of these bacteria. SFB are important indigenous bacteria for the development of the mucosal architecture and immune system in the small intestine, at least in mice. (author abst.)

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antibodies in which one of the component antibodies is directed at the T-cell receptor and the other is directed against any chosen site can focus effector T cells to function at the targeted site. We report here the production of a hybrid hybridoma cell line, H1.10.1.6, which secretes large amounts of a bispecific hybrid antibody of the IgG2a class, that can focus T-cell activity. The parental hybridoma lines for the secondary fusion were F23.1, which secretes an antibody specific for an allotypic **determinant** on the T-cell receptor of most mouse strains, and 19E12, secreting an anti-Thy-1.1 antibody. The bispecific hybrid antibody was partially purified by hydroxylapatite chromatography and characterized by isoelectric focusing. It efficiently targets Thy-1.1-expressing tumor cells for lysis by F23.1 receptor-positive **cytotoxic T-cell** clones in vitro. Such hybrid antibodies produced by hybrid hybridoma cell lines may have application in the **therapeutic** targeting of tumors or sites of viral **infections** for attack by T cells.

L10 ANSWER 22 OF 53 MEDLINE
ACCESSION NUMBER: 84282725 MEDLINE
DOCUMENT NUMBER: 84282725 PubMed ID: 6088078
TITLE: Cytolytic T cells recognize the two amino-terminal domains of H-2 K **antigens** in tandem in influenza A infected cells.
AUTHOR: Arnold B; Burgert H G; Hamann U; Hammerling G; Kees U; Kvist S
SOURCE: CELL, (1984 Aug) 38 (1) 79-87.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198409
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19840926

AB We have genetically engineered three alleles of the K locus of the major histocompatibility complex (MHC) of the mouse. These novel hybrid H-2K **genes** were introduced into mouse 1T 22-6 cells (H-2q), and their products were shown to be expressed on the cell surface. The hybrid H-2 K **antigens** were examined for their ability to function as restricting elements for **cytotoxic T lymphocytes** during influenza A **infection** . Both the alpha 1 and alpha 2 domains of the Kd **antigen** were required for T cell recognition. This implies an important role for "conformational **determinants**" on H-2 **antigens** acting as restricting elements. The cytoplasmic domain of the Kb **antigen** is not phenotypically important for recognition by T cells.

L10 ANSWER 23 OF 53 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:306130 BIOSIS
DOCUMENT NUMBER: PREV200100306130
TITLE: Posttransplantation lymphoproliferative disorders (PT-LPDs) in bone marrow and solid organ transplant recipients differ.
AUTHOR(S): Chadburn, A. (1); Hyjek, E. (1); Frizzera, G. (1); Schulman, H.; Pan, L. (1); Cesarman, E. (1); Knowles,